Antimicrobial Stewardship
in Australian Hospitals

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and **Marilyn Cruickshank**

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and Marilyn Cruickshank

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Acronyms and abbreviations

ACSQHC	Australian Commission on Safety and Quality in Health Care
ADE	adverse drug event
AMS	antimicrobial stewardship
ATC	anatomical therapeutic chemical
CAPTION	community-acquired pneumonia: towards improving outcomes nationally
CDI	*Clostridium difficile* infection
CDSS	clinical decision-support systems
CHRISP	Centre for Healthcare Related Infection Surveillance and Prevention (Queensland)
CMS	clinical microbiology service
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme
DDD	defined daily dose
DUE	drug usage evaluation
EAGAR	Expert Advisory Group on Antimicrobial Resistance
eMMS	electronic medication management system
e-prescribing	electronic prescribing
ESCMID	European Society of Clinical Microbiology and Infectious Disease
HAI	healthcare associated infection
ICU	intensive care unit
ID	infectious diseases
IT	information technology
IV	intravenous
JETACAR	Joint Expert Technical Advisory Committee on Antibiotic Resistance
MRSA	methicillin-resistant *Staphylococcus aureus*
NAUSP	National Antimicrobial Utilisation Surveillance Program
NHS	National Health Service (United Kingdom)

NPS	National Prescribing Service
OBD	occupied bed-day
PBAC	Pharmaceutical Benefit Advisory Committee
PBS	Pharmaceutical Benefits Scheme
POCI	point-of-care intervention
US	United States
WHO	World Health Organization

Acknowledgements

Executive summary

The introduction of antimicrobial agents must be considered as one of the most significant milestones in modern medicine. Previously feared and often fatal infections became curable, and the treatment seemed so safe and effective that doctors often prescribed antibiotics inappropriately for dubious indications and for longer than necessary. For many years, the emergence of resistance in some bacterial species caused little alarm, because new, more effective agents with broader antibacterial spectra were being developed. This is no longer the case. The prevalence of multidrug-resistant bacterial pathogens such as methicillin-resistant *Staphylococcus aureus* (MRSA) has risen alarmingly over the last 40 years, while in recent years few truly novel antimicrobials have been developed.

Inappropriate use of antimicrobials leads to the emergence of resistant bacteria, an increase in the risk of patient harm from avoidable adverse reactions and interactions with other drugs, infection with multiresistant bacteria or *Clostridium difficile*, and unnecessary costs.[1-3]

Most importantly, inappropriate antimicrobial use increases the risk to patients of colonisation and infection with resistant organisms and subsequent transmission to other patients. The consequences of this are now well known — patients with infections due to resistant bacteria experience delayed recovery, treatment failure and even death.[6] Turnidge et al. reported that one in five Australian and New Zealand patients diagnosed with *S. aureus* bacteraemia died, and that patients with MRSA infections had a higher mortality rate than those with methicillin-sensitive *S. aureus* infections.[6] Roberts et al. reported that twice as many patients with antimicrobial-resistant infections died than patients infected with nonresistant organisms.[5] When multiresistant pathogens are prevalent, clinicians are forced to use broader spectrum and usually more expensive agents to treat seriously ill patients. All of these effects contribute to increasing healthcare and societal costs.[5]

Research shows that up to half of antimicrobial regimens prescribed in Australian hospitals are considered inappropriate.[7-10] Compared with northern Europe, Australian hospitals have a higher overall rate of inpatient antimicrobial use. Further work is required to optimise the use of antimicrobials in our hospitals.

> As antimicrobial resistance increases and development of new antimicrobial agents declines, it is critical that antimicrobials are used wisely and judiciously.

Antimicrobial stewardship

An effective approach to improving antimicrobial use in hospitals is an organised antimicrobial management program — known as antimicrobial stewardship (AMS).[1, 11]

AMS involves a systematic approach to optimising the use of antimicrobials. It is used by healthcare institutions to reduce inappropriate antimicrobial use, improve patient outcomes and reduce adverse consequences of antimicrobial use (including antimicrobial resistance, toxicity and unnecessary costs).[12]

Effective hospital AMS programs have been shown to decrease antimicrobial use and improve patient care.[1-2] Along with infection control, hand hygiene and surveillance, AMS is considered a key strategy in local and national programs to prevent the emergence of antimicrobial resistance and decrease preventable healthcare associated infection.

Comprehensive AMS programs have demonstrated an overall reduction in antimicrobial use by 22–36%[1] and substantial pharmacy cost savings.[1-2, 4, 13] Successful programs have been shown to improve the appropriateness of antimicrobial use, and reduce institutional resistance rates, morbidity, mortality and healthcare costs.[1, 12, 14-15] Although data on the economics of AMS programs are limited, maintaining an AMS team to optimise treatment of bacteraemia has been shown to be cost-effective.[13]

The contribution of antimicrobial stewardship to the Australian Healthcare Associated Infection Program

Prevention and control of healthcare associated infection (HAI) is an essential element of patient safety and a priority area for the Australian Commission on Safety and Quality in Health Care (ACSQHC). Improving the safe and appropriate use of antimicrobials in hospitals is an important component of preventing HAI. AMS is one of several initiatives in the ACSQHC HAI program that has been identified as an important strategy to address systemic problems and gaps in the prevention of HAI. The program aims to ensure that comprehensive actions are undertaken in a nationally coordinated way by leaders and decision makers in both public and private health systems.[2]

Aim of this publication

This publication is designed to provide clinicians and health administrators with the evidence for the use of specific quality improvement and patient safety activities to reduce preventable HAI. It has been produced primarily for use in hospitals.

The publication provides guidance on developing and introducing a hospital AMS program. It describes the structure, governance and resources needed for an effective program, along with those strategies shown to influence antimicrobial prescribing and reduce inappropriate use.

Elements of antimicrobial stewardship

AMS programs are multidisciplinary: they utilise the expertise and resources of infectious diseases physicians, clinical microbiologists and pharmacists. Their success depends on the explicit support of the hospital administration, the allocation of adequate resources, and the cooperation and engagement of prescribers.

The requirements for effective AMS programs in hospitals are well described in the literature.[1, 12, 14-18] Successful programs contain a range of strategies — essential and complementary — and the structure and governance to support their implementation.

Requirements for AMS programs

Structure and governance

The overall accountability for antimicrobial management control lies with the hospital administration. They are responsible for ensuring an antimicrobial management program is developed and implemented, and outcomes are evaluated.

Hospital management support is needed, including:

- providing dedicated resources for stewardship activities, education, and measuring and monitoring antimicrobial use

- establishing a multidisciplinary AMS team with core membership (wherever possible) of either an infectious diseases physician, clinical microbiologist or nominated clinician (lead doctor), and a clinical pharmacist

- ensuring that AMS resides within the hospital's quality improvement and patient safety governance structure, and clear lines of accountability exist between the chief executive; clinical governance; drug and therapeutics, and infection prevention and control committees; and the AMS team.

Essential strategies for all hospitals

Five strategies considered essential for effective AMS in Australia are:

- implementing clinical guidelines that are consistent with the latest version of *Therapeutic Guidelines: Antibiotic*,[19] and which take into account local microbiology and antimicrobial susceptibility patterns

- establishing formulary restriction and approval systems that include restricting broad-spectrum and later generation antimicrobials to patients in whom their use is clinically justified

- reviewing antimicrobial prescribing with intervention and direct feedback to the prescriber — this should, at a minimum, include intensive care patients

- monitoring performance of antimicrobial prescribing by collecting and reporting unit or ward-specific use data, auditing antimicrobial use, and using quality use of medicines indicators

- ensuring the clinical microbiology laboratory uses selective reporting of susceptibility testing results that is consistent with hospital antimicrobial treatment guidelines.

Antimicrobial stewardship activities according to local priorities and resources

Activities that may be undertaken according to local priorities and available resources include:

- educating prescribers, pharmacists and nurses about good antimicrobial prescribing practice and antimicrobial resistance

- using point-of-care interventions, including streamlining or de-escalation of therapy, dose optimisation or parenteral-to-oral conversion

- using information technology such as electronic prescribing with clinical decision-support or online approval systems

- annually publishing facility-specific antimicrobial susceptibility data.

Structure of document

This document contains 10 chapters that summarise current evidence about AMS programs and their implementation in hospitals. The document has two parts:

1. Strategies for implementing and sustaining AMS (Chapters 1–6)

2. Resources required for AMS (Chapters 7–10).

Each chapter begins with key points and recommendations required for implementing effective AMS in hospitals. These are listed in the next section.

Key points and recommendations

1　Implementing an antimicrobial stewardship program

1.1　Key points

- Effective antimicrobial stewardship programs have been shown to improve the appropriateness of antimicrobial use, reduce patient morbidity and mortality, and reduce institutional bacterial resistance rates and healthcare costs.

- The overall accountability for antimicrobial management control lies with the hospital administration. They should be responsible for ensuring an antimicrobial stewardship program is developed and implemented, and outcomes are evaluated.

- International literature strongly suggests that the most effective approach to antimicrobial stewardship involves multidisciplinary antimicrobial stewardship teams with the responsibility and resources for implementing a program to improve antimicrobial prescribing.

- The support and collaboration of the hospital executive is essential to the success of antimicrobial stewardship teams, and clear lines of accountability to the hospital executive should be defined.

- Successful stewardship programs include a range of interventions. Two of the most effective strategies are restrictive methods, such as requiring approval to prescribe an antimicrobial, and the proactive strategy of prospective review with direct intervention and feedback to the provider.

- Teams are more likely to be effective in leading and sustaining changes in clinical practice if they have access to, and training in, effective quality improvement methods and knowledge.

1.2 Recommendations

1.2.1   Hospitals have an antimicrobial stewardship program that includes an antimicrobial prescribing and management policy, plan and implementation strategy that are regularly reviewed.

1.2.2   Hospitals have an antimicrobial formulary and guidelines for antimicrobial treatment and prophylaxis that align with *Therapeutic Guidelines: Antibiotic* and are regularly reviewed.

1.2.3   Hospitals establish a multidisciplinary antimicrobial stewardship team that is responsible for implementing the antimicrobial stewardship program. At a minimum, the team should include either an infectious diseases physician, clinical microbiologist or nominated clinician (lead doctor), and a pharmacist.

1.2.4   The antimicrobial stewardship program resides within the hospital's quality improvement and patient safety governance structure and is included within the hospital's quality and safety strategic plan.

1.2.5   Antimicrobial stewardship teams have clearly defined links with the drug and therapeutics committee, infection prevention and control committee, and clinical governance or patient safety and quality units.

1.2.6   Team members have clearly defined roles and responsibilities. Team members should be sufficiently supported and trained to enable them to effectively and measurably optimise antimicrobial use by using interventions appropriate to local needs, resources and infrastructure.

1.2.7   Antimicrobial stewardship process and outcome indicators are measured and reported to the hospital executive.

2   Formularies and antimicrobial approval systems

2.1   Key points

- Formularies can be used to influence patterns of antimicrobial use in hospitals. Each hospital should have a formulary for antimicrobial drugs, and the drug and therapeutics committee of the hospital should define rules that restrict access to particular antimicrobial agents.

- Restrictions on the use of antimicrobials have played an important role in aborting outbreaks of resistant bacteria.

- Antimicrobial approval systems have been shown to be effective in optimising antimicrobial use in a hospital setting — their use has been associated with

reduced volumes of drugs used, reduced drug costs, fewer adverse drug reactions and shorter lengths of stay.

- Approval systems may be used for preprescription or postprescription approval.

- Experts providing the approval should be members of the antimicrobial stewardship teams, or their nominees.

- Computerised systems have been found to be acceptable to clinicians as a means of facilitating antimicrobial approvals in hospitals.

2.2   Recommendations

2.2.1   Hospitals have a list of restricted antimicrobial agents and criteria for their use that is consistent with *Therapeutic Guidelines: Antibiotic*.

2.2.2   Hospitals implement an antimicrobial approval system.

2.2.3   Compliance with the approval process is audited on a regular basis.

2.2.4   Expert advice is available 24 hours a day to guide clinicians in prescribing antimicrobials.

3   Antimicrobial review and prescriber feedback

3.1   Key points

- Practice review (audit) and feedback is a proven and effective strategy to influence prescribing behaviour.

- The review of antimicrobial prescribing practice and the provision of feedback to clinicians is an essential strategy for an antimicrobial stewardship program.

- The review of antimicrobial prescribing can be prospective or retrospective.

- Prospective review can involve strategies such as pre-authorisation and antimicrobial restrictions, with feedback being provided to the prescriber before the antimicrobial is administered.

- Retrospective review occurs after antimicrobial therapy has been initiated, and facilitates the provision of feedback based on results that may not have been available at the time of initiation.

- Although evidence suggests that an antimicrobial prescribing review undertaken by a single health professional can be effective, a multidisciplinary team (e.g. including an infectious disease clinician, clinical pharmacist and microbiologist) is more likely to have a positive effect.

- Feedback should be tailored to the target audience and can be provided on a case-by-case basis or at a ward unit level.

- Provision of feedback should be structured to assist with the transfer of information.

! 3.2 Recommendations

3.2.1 Antimicrobial review and prescriber feedback is a routine part of clinical care.

3.2.2 The antimicrobial stewardship team is responsible for the provision of review and feedback at patient and unit level in wards with high antimicrobial usage (e.g. intensive care, oncology and haematology units).

4 Point-of-care interventions

4.1 Key points

- Point-of-care interventions are a valuable component of antimicrobial stewardship.

- Point-of-care interventions provide direct feedback to the prescriber at the time of prescription or laboratory diagnosis, and provide an opportunity to educate clinical staff on appropriate prescribing.

- Examples of point-of-care interventions include:
  » reviewing appropriateness of choice of antimicrobial
  » directed therapy based on microscopy and other rapid tests
  » directed therapy based on culture and susceptibility test results
  » dose optimisation
  » parenteral-to-oral conversion
  » therapeutic drug monitoring
  » automatic stop orders.

- What interventions are selected, how they are delivered and by whom, will be determined by local resources and the expertise available.

! 4.2 Recommendations

4.2.1 Point-of-care interventions are included in all antimicrobial stewardship programs.

5 Measuring the performance of antimicrobial stewardship programs

5.1 Key points

- Monitoring and analysis of antimicrobial usage is critical to understanding antimicrobial resistance and measuring the effects of stewardship interventions.

- Continuous surveillance of the appropriateness of antimicrobial prescribing should be the ultimate aim of any stewardship program.

- Reporting and analysis of ward and hospital antimicrobial usage data is useful in monitoring trends and identifying areas for evaluating appropriateness of prescribing.

- Process and outcome measures are an integral part of any quality improvement program and should be incorporated into the hospital's antimicrobial stewardship plan.

- Process indicators can be used to target and evaluate initiatives to improve prescribing. Providing timely feedback in a format that can be interpreted and used by clinicians is important.

- The introduction of an individual patient electronic medical record linked with electronic prescribing and medication management systems will improve surveillance of antimicrobial usage and appropriateness of prescribing, and enable more efficient targeting of interventions.

5.2 Recommendations

5.2.1 Antimicrobial usage data is collected and regularly reviewed to identify areas for improvement.

5.2.2 Quality indicators are monitored to assess appropriate prescribing practice and compliance with policy.

5.2.3 Information technology resources are available for:

» monitoring antimicrobial usage

» auditing process indicators

» measuring outcomes of the antimicrobial stewardship program.

5.2.4 Antimicrobial usage data is interpreted together with infection control and antimicrobial resistance data.

6 Education and competency of prescribers

6.1 Key points

- Education in safe and judicious antimicrobial prescribing is an important element of any antimicrobial stewardship program.

- Education of all health professionals involved in antimicrobial prescribing should begin at undergraduate level and be consolidated with further training throughout the postgraduate years.

- Active education techniques, such as academic detailing, consensus-building sessions and educational workshops have been shown to be more effective in changing prescribing behaviour than passive dissemination of information.

- Pharmaceutical industry-sponsored activities negatively influence prescribing behaviour.

6.2 Recommendations

6.2.1 Prescribers are taught to prescribe according to the *Therapeutic Guidelines: Antibiotic* in undergraduate, postgraduate and professional development programs.

6.2.2 Hospitals are responsible for educating clinical staff about their local antimicrobial stewardship programs.

6.2.3 Hospitals enact policies on the interaction between prescribers and the pharmaceutical industry, based on national guidance. Prescribers are educated about the influence of pharmaceutical industry activities on prescribing behaviour.

6.2.4 Education on antimicrobial stewardship is part of postgraduate training of infectious diseases physicians, microbiologists, pharmacologists, nurses and pharmacists.

7 The role of the clinical microbiology service

7.1 Key points

- The clinical microbiology service is an essential and integral part of organisational initiatives that underpin antimicrobial stewardship efforts.

- The establishment of best practice procedures for rapid microbiological evaluation is critical to delivering timely and accurate information.

- Intensive care units are an area of particular importance, as the control of resistance in these units can affect other areas of the hospital. The clinical microbiology service should therefore pay particular attention to services provided to these areas.

- Reports to the clinician from the clinical microbiology service can provide comments that interpret isolate significance, provide antimicrobial susceptibility interpretation and provide antimicrobial management advice.

- The clinical microbiology service also has a critical role to play in improving overall antimicrobial use through providing information, establishing guidelines and educating other hospital staff. One key strategy is the production of annual cumulative antibiograms to indicate susceptibility patterns for key pathogens.

- The clinical microbiology service provides surveillance data on resistant organisms for infection control purposes.

7.2 Recommendations

7.2.1   Hospitals have access to a clinical microbiology service that provides:

» best practice diagnostic testing for infection, including relevant rapid tests for common viral, fungal or bacterial pathogens that are reported to clinicians

» consultation on choice, nature, handling and testing of specimens for detection of infection, especially when there is a broad infectious differential diagnosis under consideration

» direct advice from a specialist consultant or supervised registrar to clinicians at the time when bloodstream, meningeal or other critical infection is detected (this should occur seven days per week)

» regular patient-specific liaison with clinicians (including infectious diseases physicians if they are not integrated with the clinical microbiology service) who care for patients at a high risk of infection (e.g. patients in intensive care, haematology and oncology units).

7.2.2   Regular analyses of antimicrobial resistance are provided to groups with responsibility for local antimicrobial guidelines (e.g. antimicrobial stewardship committee, drug and therapeutics committee) to inform local empirical therapy recommendations and formulary management.

7.2.3   Cascade reporting of antimicrobial susceptibility is consistent with the *Therapeutic Guidelines: Antibiotic.*

7.2.4   A national standard approach to antimicrobial susceptibility testing and cumulative analysis and reporting of antibiograms is developed, agreed and implemented by clinical microbiology services.

8 The role of the infectious diseases service

8.1 Key points

- Infectious diseases physicians give legitimacy to antimicrobial stewardship programs and play an important role by collaborating with local specialists to ensure that the team's goals are understood and met.

- The infectious diseases service makes an important contribution to formulary decision making, antimicrobial restriction policies, and the establishment and operation of antimicrobial approval systems.

- The infectious diseases service has a critical role in improving overall antimicrobial use through providing expert advice on the appropriate use of antimicrobials, education of prescribers, and developing and implementing evidence-based guidelines for antimicrobial treatment and prophylaxis as part of the antimicrobial stewardship team.

8.2 Recommendations

8.2.1   The antimicrobial stewardship team includes an infectious diseases physician or clinical microbiologist (if available).

8.2.2   Hospitals have access to an infectious diseases service that provides expert advice, educates prescribers, and plays a major role in the development and implementation of antimicrobial policy and prescribing guidelines.

8.2.3   Hospitals without an on-site clinical microbiologist or infectious diseases physician negotiate external support for antimicrobial stewardship activities.

9 The role of the pharmacy service

9.1 Key points

- Pharmacists are essential to the success of antimicrobial stewardship programs and have a positive effect on improving appropriate antimicrobial use, patient care and safety.

- Hospital pharmacists are well placed to prospectively or retrospectively review antimicrobial orders, provide feedback to prescribers, and identify cases requiring review and referral to the nominated antimicrobial stewardship health professional or team.

- A pharmacist with experience and training in antimicrobial stewardship is a key member of the antimicrobial stewardship team. Their prime role is to champion

and coordinate the activities of the hospital's antimicrobial stewardship program in collaboration with the antimicrobial stewardship program leader.

- The responsibilities of pharmacists in antimicrobial stewardship include:
    - » providing expert advice and education to relevant hospital staff
    - » contributing to ward rounds, consultations and relevant hospital committees (e.g. antimicrobial stewardship committee or drug and therapeutics committee)
    - » participating in policy development and the application and maintenance of antimicrobial formulary and prescribing guidelines
    - » implementing and auditing activities that promote safe and appropriate use of antimicrobials
    - » being involved in research activities related to antimicrobial stewardship.

9.2   Recommendations

9.2.1   The antimicrobial stewardship team includes a pharmacist who has experience or is trained in antimicrobial stewardship, and who is allocated time and resources for antimicrobial stewardship activities.

9.2.2   Pharmacists review antimicrobial orders for adherence to local guidelines and provide timely feedback (where applicable) to the prescriber.

9.2.3   Pharmacists are supported by the hospital in enforcing antimicrobial prescribing policies, including formulary restrictions and encouraging adherence to local prescribing guidelines.

9.2.4   Hospitals support training for pharmacists to equip them with the knowledge and skills required to effectively participate in antimicrobial stewardship activities.

9.4.5   Mechanisms are in place to allow pharmacists to seek expert advice from, and refer to, a clinical microbiologist or infectious diseases physician.

10 Use of computer technology to support antimicrobial stewardship

10.1 Key points

- Electronic clinical decision-support systems are potentially useful tools in antimicrobial stewardship programs.

- Organisational, social and cultural issues relating to prescribing behaviour are key factors that determine the effectiveness of these systems, and resources should be directed towards addressing these issues during implementation.

- Electronic decision support must be integrated into the clinical workflow to be effective in a complex clinical domain such as antimicrobial prescribing.

- Electronic stewardship systems are most likely to be successful as part of a multidisciplinary antimicrobial stewardship program.

10.2 Recommendations

10.2.1 Hospitals work towards implementing electronic decision-support systems to guide antimicrobial prescribing and integrating these systems with electronic health records, and electronic prescribing and medication management systems.

10.2.2 An antimicrobial stewardship pharmacist and antimicrobial stewardship team are available to support and maintain electronic stewardship systems.

10.2.3 Antimicrobial stewardship teams have access to patient administrative data, microbiology data (including antimicrobial resistance) and drug use data for monitoring and reporting purposes.

Introduction

Authors: Lyn Gilbert and Margaret Duguid

Background

The introduction of antimicrobial agents has been one of the most significant developments in medicine; it has contributed to the demise of infectious diseases as the major cause of premature death. Previously feared and often fatal infections became 'miraculously' curable. Indeed, treatment with antimicrobial agents seemed so effective and safe that doctors often prescribed antimicrobials for dubious indications and for longer than necessary, with little concern for adverse effects. For many years, the emergence of antimicrobial resistance in some bacterial species caused little alarm, because new and more effective agents with broader antibacterial spectra were being developed.

However, in the last 40 years, the prevalence of multidrug-resistant bacterial pathogens, such as methicillin-resistant *Staphylococcus aureus* (MRSA), has risen alarmingly. Initially, this occurred mainly in hospitals, but now it is happening increasingly in the community. Unnecessary antimicrobial use for self-limiting or noninfective illness, and inappropriate antimicrobial choice, dose or duration of therapy drive the selection of resistant bacteria, disrupt normal microbial flora, and increase the risk of colonisation with resistant organisms and subsequent transmission to others.

In addition, the pace of antimicrobial development has slowed markedly in the past 20 years.[12] Few truly novel antimicrobials have been developed in recent years and it is expected that there will be a minimal number of new agents introduced in the next decade.[12, 20] As well as the technical challenges in the development of new drugs, there is little incentive for pharmaceutical companies to invest in such development when the use of antimicrobials is becoming increasingly (and appropriately) restricted.

Inappropriate antimicrobial use increases morbidity and mortality due to avoidable drug toxicity, suboptimal treatment of the original infection, or subsequent infection with multiresistant bacteria, fungi or *Clostridium difficile*. Patients with antimicrobial-resistant infections are more likely to experience ineffective treatment, recurrent infection, delayed recovery or even death. An all-cause mortality rate of 20.6% at 30 days in Australian and New Zealand patients diagnosed with *S. aureus* bacteraemia has been reported, and MRSA infections are associated with a higher mortality than infections due to methicillin-sensitive *S. aureus*.[6] A two-fold higher death rate has been reported among patients with antimicrobial-resistant infections.[5]

There is good evidence that overall rates of antimicrobial resistance correlate with the total quantity of antimicrobials used, as determined by the number of individuals treated and the average duration of each treatment course. Some antimicrobials promote the emergence of resistance more than others, depending in part on the breadth of their antimicrobial spectrum. In individuals, the risk of colonisation and infection with multiresistant bacteria correlates strongly with previous antimicrobial therapy.

Data collected through the National Antimicrobial Utilisation Surveillance Program (NAUSP) in 2007–08 demonstrate a higher overall use of inpatient antimicrobials in Australian hospitals compared with overall use in hospitals in northern Europe. Although these data are incomplete — they represent only 48% of Australian principal referral (major city) centres — Australian use rates in hospitals are particularly high for some antimicrobial classes, including those known to promote the emergence of resistance, such as cephalosporins and macrolides (see Appendix 1). There is also unexplained wide variation in usage rates for broad-spectrum antimicrobials.

Up to 50% of antimicrobial courses prescribed in hospitals overseas and in Australia are considered inappropriate.[1, 4, 7-10, 13, 21-22] Antimicrobials are still used unnecessarily and inappropriately, despite the availability of well-established, evidence-based treatment guidelines. The reasons for this vary. Like other ecological problems, antimicrobial resistance develops slowly and, although much is known about the causes, it is difficult to attribute the effects to specific actions or decisions.

Doctors may be unaware that guidelines are available or too busy to consult them. They may be confident that they know the best antimicrobial choice, or are unconvinced of the risks entailed in their inappropriate use. Many doctors are unwilling to withhold antimicrobial therapy if the diagnosis is uncertain, or to risk treatment failure by using a narrow-spectrum agent. Courses of antimicrobials are often continued for longer than necessary because prescriptions are not time-limited and no-one remembers to cancel them.

When multiresistant pathogens are prevalent, clinicians are forced to use broader spectrum and (usually) more expensive agents for empirical therapy for seriously ill patients with sepsis. All of these effects contribute to increasing healthcare and societal costs. In 2009, medical costs in the United States attributable to antimicrobial-resistant infections were estimated at US$18 500–29 000 per patient, and were associated with an excess length of hospital stay of 6.4–12.7 days.[5]

Antimicrobial management or stewardship programs have developed as a response to these issues. As antimicrobial resistance increases and the development of new antimicrobial agents declines, it is critical that we use antimicrobials that are still effective wisely and judiciously. Antimicrobial stewardship (AMS) is a systematic approach to optimising the use of antimicrobials. It is used by healthcare institutions to reduce inappropriate antimicrobial use, improve patient outcomes and reduce adverse consequences of antimicrobial use (including antimicrobial resistance, toxicity and unnecessary costs).[12]

These programs aim to change antimicrobial prescribing behaviour. They have been shown to reduce unnecessary use, improve patient outcomes and promote the use of agents less likely to select for resistant bacteria.[23] Effective stewardship programs can lead to an overall reduction in antimicrobial use by 22–36%[1] and substantial pharmacy cost savings;[1-2, 13] they can reduce resistance rates in institutions and the morbidity, mortality and excess costs of healthcare associated infections (HAI).[24] Although there are limited data on the economic benefits, maintaining an AMS team to optimise treatment of bacteraemia has been shown to be cost-effective.[13]

AMS programs are multidisciplinary, using the expertise and resources of infectious diseases (ID) physicians, clinical microbiologists and pharmacists. Their success depends on the explicit support of hospital administration, allocation of adequate resources, and the cooperation and engagement of prescribers. If we expect antimicrobial prescribing to improve, we must provide prescribers with information in an accessible and locally relevant format. This includes easy access to:

- antimicrobial guidelines and active educational programs

- regularly updated local antimicrobial resistance data

- rapidly available patient-specific laboratory results at the point of care

- decision-support tools and regular expert consultation to assist in the choice of antimicrobial regimen

- review and feedback on the appropriateness of antimicrobial prescribing.

This book describes the elements of effective AMS programs and the evidence to support their inclusion in hospital quality and safety programs.

The contribution of antimicrobial stewardship to the Australian Healthcare Associated Infection Program

Prevention and control of HAI is an essential element of patient safety. It is one of the priority areas for the Australian Commission on Safety and Quality in Health Care (ACSQHC). ACSQHC's HAI Program, established in 2007, aims to develop a national approach to reducing HAI in Australia. This includes identifying and addressing systemic problems and gaps, to ensure that comprehensive actions are undertaken in a nationally coordinated way by leaders and decision makers in both public and private health systems.

Part of the prevention and control of HAI is improving the safe and appropriate use of antimicrobials through AMS. Along with infection control, hand hygiene and antimicrobial surveillance, AMS is a key project in the ACSQHC HAI Program to prevent and contain antimicrobial resistance.[2] This book is one of several initiatives within the HAI Program, designed to provide clinicians and health administrators with evidence for the use of specific quality improvement and patient safety activities to reduce preventable HAI. It is the first of several initiatives within ACSQHC's Antimicrobial Stewardship Advisory Committee's program of work.

Elements of antimicrobial stewardship

The requirements for effective AMS programs in hospitals are well described in the literature.[1, 12, 14-17] Minimum AMS measures have been developed[16] and evidence-based guidelines[1] and recommendations published for good antimicrobial practice in hospitals.[17-18] Successful programs contain a range of strategies — essential and complementary — and the structure and governance to support their implementation. Requirements for AMS programs in Australian hospitals are outlined in Chapter 1.

Structure of this document

This document contains 10 chapters that summarise current evidence about AMS programs and their implementation in hospitals. The document has two parts:

1. Strategies for implementing and sustaining AMS (Chapters 1–6)
2. Resources required for AMS. (Chapters 7–10)

Key points and recommendations detail the requirements for effective antimicrobial stewardship, and are given at the start of each chapter and in the executive summary.

Part 1   Strategies for antimicrobial stewardship

The six chapters in Part 1 cover the implementation of an AMS program and the various strategies for influencing safe and appropriate prescribing of antimicrobials in hospitals.

Chapter 1 looks at the implementation of AMS on an institution-wide basis, and details what constitutes a stewardship program, the governance of such a program, and the staff, resources and leadership required to effect change. How to go about forming an AMS team and fomulating an implementation strategy is discussed, and an example of a successful Australian program is provided.

Chapters 2 and 3 examine two key strategies to improve antimicrobial prescribing: formulary restriction and approval systems, and review with feedback to prescribers. These strategies are considered to be the most effective interventions in achieving safe and appropriate prescribing, and are core components of any successful AMS program.

Evidence is presented for the use of a formulary system that contains a list of restricted antimicrobial drugs that require prior approval for use, endorsed by the hospital's drug and therapeutics committee. Antimicrobial approval systems are discussed and the form and effectiveness of various systems, including electronic systems, is examined.

The benefits of prospective and retrospective review of antimicrobial orders for individual patients, and the provision of feedback to prescribers, are presented along

with a discussion on responsibilities for reviews and the presentation of feedback. Antimicrobial review and prescriber feedback should be routine and organisational reviews should be part of quality improvement activities.

Chapter 4 examines point-of-care interventions that provide feedback to the prescriber from the stewardship team, ID physician, microbiologist or pharmacist on the management of individual patients. In addition to improving patient management (and sometimes outcomes), point-of-care interventions provide good opportunities to educate clinical staff on rational prescribing. Examples of point-of-care interventions include directed therapy, dose optimisation and parenteral-to-oral conversion.

Chapter 5 follows on from the analysis presented in Chapters 2 and 3, and looks at the effective use of antimicrobial use data, including large-scale reporting and analysis of hospital dispensing data, to monitor trends and identify areas for more intensive drug usage evaluation. The value of point prevalence studies in measuring the quality of prescribing is discussed, as is the importance of using process and outcome indicators to measure the effectiveness of stewardship activities.

Chapter 6 covers what is needed to ensure the competency of antimicrobial prescribers, including educational strategies, programs and resources. Education is an essential element of any AMS program. It should begin at undergraduate level and be consolidated throughout postgraduate study, and include the use of evidence-based guidelines and specific education on AMS. Factors influencing prescribing also need to be addressed, including the effect of pharmaceutical company promotional activities. Examples of overseas programs and strategies for continuing education are presented in the chapter.

Part 2   Resources required for antimicrobial stewardship

Chapters 7–9 examine in detail the roles of specific hospital services in AMS: Chapter 7 addresses the clinical microbiology service; Chapter 8, the infectious diseases service; and Chapter 9, the pharmacy service.

Finally, Chapter 10 looks at how hospitals are changing, and the integration of AMS programs into electronic decision-support systems and new technology platforms, such as electronic prescribing and electronic medicines management systems. The importance of integrating antimicrobial prescribing into clinical workflow is discussed, along with the need to provide adequate resources to support electronic stewardship systems.

Appendix 1 contains 'Antimicrobial usage: monitoring and analysis', Chapter 15 from: *Reducing Harm to Patients from Health Care Associated Infection: the Role of Surveillance*, edited by M Cruickshank and J Ferguson, and published by ACSQHC in 2008.[2]

Appendix 2 contains a range of AMS resources, including examples of guidelines from Australian hospitals, AMS web sites and guidelines on managing relationships with the pharmaceutical industry.

Part I

Strategies for implementing and sustaining antimicrobial stewardship

1 Implementing an antimicrobial stewardship program

Authors: Helen van Gessel and Margaret Duguid

1.1 Key points

- Effective antimicrobial stewardship programs have been shown to improve the appropriateness of antimicrobial use, reduce patient morbidity and mortality, and reduce institutional bacterial resistance rates and healthcare costs.

- The overall accountability for antimicrobial management control lies with the hospital administration. They should be responsible for ensuring an antimicrobial stewardship program is developed and implemented, and outcomes are evaluated.

- International literature strongly suggests that the most effective approach to antimicrobial stewardship involves multidisciplinary antimicrobial stewardship teams with the responsibility and resources for implementing a program to improve antimicrobial prescribing.

- The support and collaboration of the hospital executive is essential to the success of antimicrobial stewardship teams, and clear lines of accountability to the hospital executive should be defined.

- Successful stewardship programs include a range of interventions. Two of the most effective strategies are restrictive methods, such as requiring approval to prescribe an antimicrobial, and the proactive strategy of prospective review with direct intervention and feedback to the provider.

- Teams are more likely to be effective in leading and sustaining changes in clinical practice if they have access to, and training in, effective quality improvement methods and knowledge.

1.2 Recommendations

! 1.2.1 Hospitals have an antimicrobial stewardship program that includes an antimicrobial prescribing and management policy, plan and implementation strategy that are regularly reviewed.

1.2.2 Hospitals have an antimicrobial formulary and guidelines for antimicrobial treatment and prophylaxis that align with *Therapeutic Guidelines: Antibiotic*[19] and are regularly reviewed.

1.2.3 Hospitals establish a multidisciplinary antimicrobial stewardship team that is responsible for implementing the antimicrobial stewardship program. At a minimum, the team should include either an infectious diseases physician, clinical microbiologist or nominated clinician (lead doctor), and a pharmacist.

1.2.4 The antimicrobial stewardship program resides within the hospital's quality improvement and patient safety governance structure and is included within the hospital's quality and safety strategic plan.

1.2.5 Antimicrobial stewardship teams have clearly defined links with the drug and therapeutics committee, infection prevention and control committee, and clinical governance or patient safety and quality units.

1.2.6 Team members have clearly defined roles and responsibilities. Team members should be sufficiently supported and trained to enable them to effectively and measurably optimise antimicrobial use by using interventions appropriate to local needs, resources and infrastructure.

1.2.7 Antimicrobial stewardship process and outcome indicators are measured and reported to the hospital executive.

1.3   Antimicrobial management programs

Antimicrobial management programs in hospitals, known as antimicrobial stewardship (AMS) programs, have been developed in response to the emergence of antimicrobial resistance in pathogens encountered in hospitals and — more recently — in the community. Improving the safe and appropriate use of antimicrobials is an important component of patient safety in hospitals[11] and there is extensive evidence for the efficacy of AMS. Together with infection prevention and control, hand hygiene and healthcare associated infections (HAI) surveillance, AMS is considered a key component of a multifaceted, multidisciplinary approach to preventing the emergence of antimicrobial-resistant pathogens and decreasing preventable HAI.

AMS has been defined as 'an ongoing effort by a health-care institution to optimise antimicrobial use among hospital patients in order to improve patient outcomes, ensure cost-effective therapy and reduce adverse sequelae of antimicrobial use (including antimicrobial resistance)'.[12] Successful AMS programs have been shown to improve the appropriate prescription of antimicrobials and reduce institutional resistance rates, morbidity, mortality and healthcare costs.[1, 3, 12, 22, 24] AMS programs are multidisciplinary, using the expertise and resources of infectious diseases (ID) physicians, clinical microbiologists, infection control practitioners and pharmacists. Their aim is to change antimicrobial prescribing to reduce unnecessary use and to promote the use of agents less likely to select resistant bacteria. This is done in line with treatment guidelines and with consideration of the demonstrated local incidence of antimicrobial-resistant pathogens (as shown by antibiograms).[25]

This chapter will focus on how to develop and implement an antimicrobial management program in hospitals and the role of the AMS team in establishing and implementing the program.

1.4   Effective implementation of antimicrobial stewardship programs

A significant percentage of improvement programs in health care do not succeed, fail to be implemented throughout an organisation or are not sustainable. These include interventions that are based on excellent technical evidence and that have been successful in other locations and contexts — such as the AMS strategies described in this book.

Successfully influencing clinical practices, such as antimicrobial prescribing in hospitals, is complex. To maximise the chance of success, AMS teams are urged to learn about and incorporate findings from other quality improvement work in health care.

Boaden et al.[26] recently summarised the factors associated with successful improvement of clinical processes and outcomes in health care:

- participation of a nucleus of physicians

- feedback to individual practitioners

- supportive organisational culture

- conducive external environment

- phased and coordinated approach to spreading interventions where management monitors progress, coordinates team efforts and allocates resources

- bottom-up activities supported by top-down policies that are consistent with the improvement objectives.

There are also principles of improvement that should guide the process of AMS program development and implementation. They are:

- knowing what needs to be improved and having a clear aim that will guide the effort and motivate participants

- making sure there is a process to get feedback to let participants know if improvement is happening and if changes are being made that are taking them closer to their aim

- developing changes that are likely to make improvements

- testing a change before any attempts are made to implement it permanently by using some form of experiential learning method, such as the Plan-Do-Study-Act cycle

- knowing when and how to implement a permanent change.[27]

These principles are integrated into relevant sections of this and other chapters of this book as appropriate. Readers are urged to seek further information and training in quality improvement if they do not have access to relevant expertise. There are many useful resources, including the NSW Health publication, *Easy guide to clinical practice improvement*[28] and the Institute for Healthcare Improvement.[a]

1.5   The evidence for antimicrobial stewardship programs

The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America collaboratively reviewed AMS strategies. The review showed that comprehensive AMS programs consistently demonstrated a decrease in antimicrobial use (in the order of 22–36% reduction) and significant cost savings.[1] Similarly, authors systematically reviewed 66 studies on AMS interventions for the Cochrane Collaboration. They reported improved drug use in 81% of the studies that examined optimising antimicrobial use.[22]

Reducing unnecessary antimicrobial use and optimising treatment minimises the potential for selecting resistant organisms.[14-15] There are many examples where changes in antimicrobial prescribing practices have had a significant effect on outbreaks of resistant pathogens.[22, 29] However, these programs are often implemented in times of crisis, such as in response to the emergence of resistance in a unit or hospital. There are few studies examining the effect of an established AMS program on the emergence of resistant organisms over long time periods.

a   www.ihi.org

One large study of 448 hospitals in the United States found an inverse relationship between the presence of AMS programs and local antimicrobial resistance rates. This study showed high implementation rates of guideline-recommended practices, and optimising the duration of empirical therapy were associated with a lower prevalence of resistant organisms.[30] Some of the most successful AMS programs reported have been those that aimed to reduce *Clostridium difficile* infection (CDI) rates.[22] A number of studies have demonstrated that reducing the overall use of antimicrobials, combined with improved infection control precautions, reduces the incidence of nosocomial CDI.[15, 29, 31] Figure 1.1 provides an example of the outcome of a program of improved infection control and targeted antimicrobial consumption on CDI incidence in a Canadian hospital.[31]
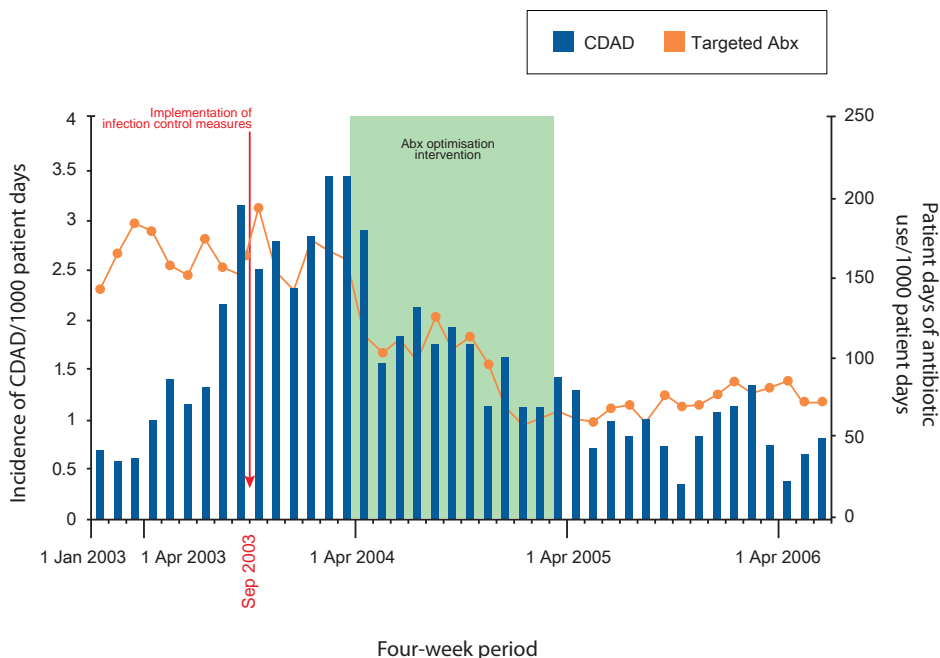
Source: Valiquette et al. (2007)[31]

Figure 1.1   Targeted antibiotic (Abx) consumption and nosocomial *Clostridium difficile*-associated disease (CDAD) incidence per 1000 patient days of hospitalisation

Inadequate antimicrobial therapy is associated with increased patient morbidity and mortality due to infection,[3, 32] and is an independent risk factor for death among critically ill patients with severe infection.[32] In addition to improving patient care by reducing the risk of HAI, programs that improve antimicrobial prescribing have been shown to increase cure rates, decrease treatment failures[14] and decrease mortality from infection.[22, 33] In the Cochrane Collaboration's systematic review, 26% of the studies reported microbiological outcomes and, of these, 75% reported significant improvements in the local bacterial resistance rates.[22] A smaller number of studies (nine) also reported on clinical outcomes (length of hospital stay, mortality) and the majority reported improvement. The authors concluded that interventions to improve antimicrobial prescribing to hospital inpatients are successful in reducing

antimicrobial resistance in local pathogens, and decreasing the incidence of HAI, death, illness and length of hospital stay.

Implementation of any new program requires some financial investment; however, published studies indicate that AMS programs at least cover their costs and can be financially self-supporting.[1, 12] Examples of interventions that have direct cost savings include:[15]

- stopping antimicrobial administration when patients are no longer infected

- switching from intravenous to oral therapy

- de-escalating from broad-spectrum combination therapy to directed therapy.

Maintaining an AMS team with the focused objective of optimising treatment of bacteraemia as a single infective syndrome has been shown to be cost-effective.[13] Dellit et al. describe annual savings of US$200 000–900 000 in large teaching hospitals and small community hospitals with multidisciplinary antimicrobial management programs.[1] Similar savings have been reported in Australia (see Box 4 in this chapter and Case study 2 in Appendix 1).

1.6 Governance of antimicrobial stewardship programs

The appropriate use of antimicrobials is considered an essential part of patient safety, thus requiring careful oversight and guidance.[1, 11] ACSQHC supports recommendations that the AMS program should reside within the hospital quality improvement and patient safety governance structure,[1, 17] and be included within the hospital's quality and safety strategic plan.[3]

As AMS is an important component of patient safety, its performance indicators should be safety and quality parameters that can be measured, and for which hospital and hospital executives should be accountable.

The responsibility for implementing and managing the program should reside with a multidisciplinary AMS team or committee.[1, 17-18] Formal links should be established between the:

- AMS team

- hospital executive

- director of clinical governance

- drug and therapeutics committee

- infection prevention and control committee.[1, 17]

The AMS team should be represented on the last two committees.[1]

It is desirable that antimicrobial stewardship programs function under the auspices of quality assurance and patient safety.[1]

Figure 1.2 is an example of a reporting framework for an AMS team established for Scottish hospitals.[17] The structure emphasises that AMS is an important component of patient safety that must be integrated into the local clinical governance and patient safety framework. This model could be adapted to the varying Australian hospital structures in place.
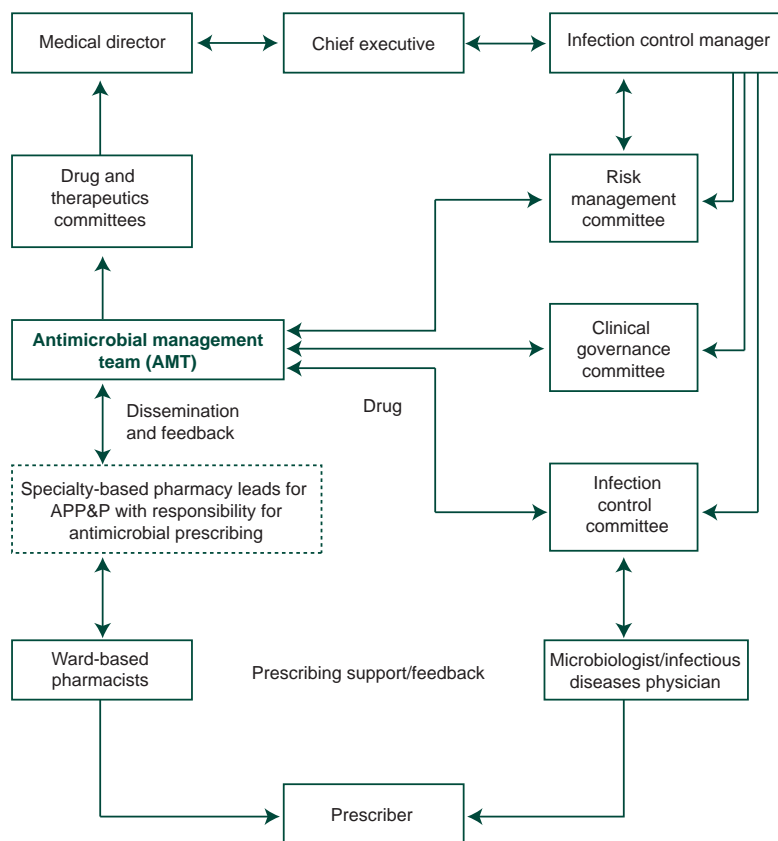
APP&P = antimicrobial prescribing policy and practice
Source: Nathwani (2006)[17]

Figure 1.2   Model for antimicrobial prescribing pathways in acute hospitals (Scotland)

1.6.1   The role of hospital executives in antimicrobial stewardship

Like any change and improvement activity, the success of the AMS program is dependent on the support and leadership of hospital management and senior medical staff.[1, 16-17] Without support from hospital leadership, funding may be inadequate and prescribers may thwart attempts to improve antimicrobial use.[12]

Hospital leaders can demonstrate their explicit support for improvements such as AMS programs by:

- allocating an executive sponsor
- making AMS a strategic goal of the organisation
- communicating why change is needed to staff and other leaders
- scheduling time to review progress and provide advice
- assigning high-performing staff to the team and resourcing them adequately.[27]

1.7   The antimicrobial stewardship team

Multidisciplinary teams are better suited to implement the kind of improvement and change required for effective AMS.[34] There are a range of professions and individuals that have an interest in and responsibility for AMS, each with different perspectives and skills. Involving prescribers, pharmacists, administrators, infection control experts, information systems experts, microbiologists and ID physicians into a well-managed team effectively incorporates their views and expertise.

As a minimum, a multidisciplinary AMS team or committee should include an appropriate clinician (a microbiologist or ID physician, if available) and a clinical pharmacist (with ID training, if possible) as core team members.[1, 16-17, 34]

Where on-site ID physicians or clinical microbiologists are not available, the AMS team should be lead by an interested clinician with a clinical pharmacist. In these circumstances, hospitals should negotiate appropriate external specialist advice to support the local AMS team. Small hospitals without an on-site pharmacist should be able to seek advice from a clinical pharmacist (e.g. from a regional hospital).

Core team members should have dedicated time for AMS tasks. One group from the United States suggested that in hospitals with more than 150 beds, a full-time pharmacist and part-time physician are required, with less staffing for institutions with 100–150 beds.[35] There is no consensus on staffing recommendations in Australia. However, clinicians in hospitals with existing programs suggest that for every 100 acute beds, at least 10 hours (0.3 full-time equivalent) of senior pharmacist and 3.5 hours (0.1 full-time equivalent) of lead clinician time per week should be dedicated to AMS activities (K Buising, Infectious Diseases Physician, St Vincent's Hospital, Melbourne, Clinical Research Physician Victorian Infectious Diseases Service, Royal Melbourne Hospital, pers comm, 2010).

Quality antimicrobial prescribing should be a strategic goal of hospital executives and an objective of clinical governance:

The public health aspects of antibiotic resistance necessitate that executive responsibility be taken for antimicrobial prescribing in future. For the doctor making the prescribing decision on any individual patient, it is often difficult to balance the various aspects of the decision making process. It is essential that the burden of some of the responsibilities be borne by the institution such that spiralling therapeutic empiricism does not dominate the decision making process, resulting in unnecessary broad spectrum treatment in order to cover 100% of possible pathogens.[16]

The support and collaboration of hospital administration, medical staff leadership, and local providers in the development and maintenance of antimicrobials stewardship programs is essential.[1]

The core team members should recruit others as appropriate. Colleagues from a range of clinical disciplines may assist in developing strategies that are more acceptable to prescribers. This may also help to engage a broad range of prescribers in AMS activities. Team members should be clear about their roles and their time commitment. An example of an AMS program team terms of reference is provided in Appendix 2, Section A.2.1.

Team membership should not be confined to those with professional expertise in antimicrobial usage. Evidence from quality improvement work suggests that effective improvement teams include members with three broad kinds of expertise and authority:

- a system leader who has the authority to institute change and overcome barriers (e.g. a senior member of clinical administration)

- an individual with technical expertise, such as an ID physician, pharmacist or microbiologist

- someone to provide day-to-day leadership with dedicated time allocation. This is the driver of the project who ensures implementation and performance measurement. An AMS team comprised solely of technical experts is less likely to be able to effect change and improvement. In an AMS team, this person could have one of a variety of professional backgrounds, including a pharmacist with training in quality improvement, or a member of the safety and quality team.

The AMS team should establish links with existing committees or groups, have representation on the drug and therapeutics committee, and the infection prevention and control committee, and seek endorsement of the hospital executive for formal structural alignment (see Figure 1.2).

1.8 The antimicrobial stewardship program plan

Once executive support, the AMS team and a governance structure are established, the next step is to plan the AMS program.

The AMS team will have to develop clear aims and metrics that allow monitoring of improvements, and select changes to consider and test for implementation. An AMS policy will need to be developed or updated to underpin these activities. The AMS team should consider whether to develop this policy as their first activity, or in parallel with investigating and testing changes aimed at improved prescribing. As the policy development process can be a useful way to gain multidisciplinary input and engagement, initially focusing on this activity is likely to be particularly important if there has been little progress in AMS to date. However, AMS teams should try to avoid extremely prolonged policy development to the exclusion of other activities, as this will slow progress in developing and testing systems to directly influence antimicrobial prescribing. AMS policy is discussed further in Section 1.9.

Gathering information to better understand the local organisational culture is essential to maximising a new AMS program's chances of success. This information

should be used to inform testing and implementation, and to build a business case for resourcing, if required. An approach to setting up an AMS program is outlined below, and it is highly recommended that any hospital introducing or strengthening AMS in their institution consider following these steps:

1. Collect baseline information relevant to the institution

    » antimicrobial use and trends over time

    » antimicrobial expenditure and trends over time

    » the institution's microbial susceptibility patterns.

2. Assess organisational culture regarding AMS — readiness survey, what the local 'drivers' are (e.g. financial savings, antimicrobial resistance), and the level of executive support or commitment to the program.

3. Assess what assets are available (e.g. interested personnel, trained personnel, information technology support and willingness to look at new systems, microbiology, ID physician and pharmacy availability and support). Assess what resources are accessible (e.g. this book, jurisdictional guidelines, latest version of *Therapeutic Guidelines: Antibiotic,*[19] web sites, other groups, state therapeutic advisory group resources). Appendix 2 provides information on resources and useful web sites.

4. Review existing antimicrobial prescribing and management policies. Assess if they are current, comprehensive, and whether they have been audited and cover all the necessary issues or not (see Section 1.9). Ensure that the policy nominates a person and their position within the hospital who has executive responsibility for the policy content, implementation and monitoring, and that this person will be involved in future AMS activities. Ensure the policy is readily available to all healthcare professionals in hard copy or online.

5. Review the existence, accessibility and acceptance of the organisation's antimicrobial treatment and surgical prophylaxis guidelines. Assess whether or not the guidelines

    » are consistent and evidence based

    » reflect agreed best practice (e.g. as stated in *Therapeutic Guidelines: Antibiotic*[19])

    » specify recommended agent, dose, route and duration of empirical antimicrobial treatment for the major infection categories.

6. Review existing groups or committees with an interest in AMS (e.g. safety and quality, drug and therapeutics, infection prevention and control, postgraduate medical education committees). Their responsibilities and reporting structures should be understood, as well as how they might impact or interact with AMS work.

7. Review the organisation's existing communication strategies, particularly those aimed at prescribers (e.g. access and use of email, newsletters, departmental meetings, mobile phones).

An institution's readiness to adopt an AMS program is discussed in Chapter 2, including how to implement electronic decision-support and approval systems.

1.9 Antimicrobial prescribing and management policy

An antimicrobial prescribing and management policy should be in place and used as a base for education programs. It should have an expiry date and be regularly reviewed and audited. As mentioned in Section 1.8, policy development is likely to be particularly important in sites just beginning an AMS program. The policy should be developed by the AMS team and approved by the drug and therapeutics committee. Prescribers should have easy access to it, including electronically (preferably) and a printed version.[36] As a minimum, the policy should include:

- the requirement for clinicians to prescribe antimicrobials guided by the latest version of the *Therapeutic Guidelines: Antibiotic*[19] wherever possible, with specific mention of how evidenced-based practice recommendations for antimicrobial prescribing are to be applied locally

- a list of restricted antimicrobials and the procedures for obtaining approval for these

- guidelines for prescribing, including local clinical guidelines

- reference to the hospital's policy on liaising with the pharmaceutical industry.

An example template for a hospital antimicrobial policy prepared by the Specialist Advisory Committee on Antimicrobial Resistance (SACAR) in the United Kingdom is provided in Appendix 2. Appendix 2 also includes examples of Australian policies. A summary of the SACAR template contents is provided in Box 1.

Prescribing policies should accord with *Therapeutic Guidelines: Antibiotic*[19] and incorporate messages such as the antimicrobial creed, MINDME (see Box 2).

The United Kingdom Department of Health's *Antimicrobial prescribing: summary of best practice* also provides recommendations that could be incorporated into prescribing policy:[18]

- *Decision to prescribe.* The decision to prescribe an antimicrobial should always be clinically justified and the reason(s) recorded in the patient's medical record. It is important not to prescribe antimicrobials on a 'just in case' basis. Antimicrobials prescribed empirically in life-threatening situations should be reviewed early in light of factors such as microbiological results and clinical progress, and, where necessary, changed or discontinued as soon as is reasonable.

- *Intravenous (IV) or oral therapy.* Unless there are not suitable alternatives, IV therapy should only be used for those patients with severe infections or who are unable to take oral antimicrobials. As a general rule, IV antimicrobials should only be prescribed for two days, after which the prescription should be reviewed and, if appropriate, the patient switched to an oral equivalent.

- *Review of antimicrobial treatment.* It is important to establish a culture that includes daily review and de-escalation from IV to oral therapy. It should set maximum durations for treatment without repeat prescription, unless there is a clear indication in the medical record that antimicrobials should be continued (e.g. a specific infection that requires extended therapy). The patient's microbiology results should be reviewed regularly and antimicrobial therapy rationalised accordingly. In a critical care environment, for example, a joint daily round between intensivist, microbiologist and pharmacist should be considered.

- *Minimising use of broad-spectrum antimicrobials.* The use of broad-spectrum antimicrobial agents is a major factor in inducing CDI. Therefore, clinicians should

avoid the widespread use of cephalosporins, quinolones, broad-spectrum penicillins and clindamycin unless there are clear indications for their use. Broad-spectrum antimicrobials should be restricted to the treatment of serious infections when the pathogen is not known or when other effective agents are unavailable. Restricted antimicrobials should not be held in main ward stocks and should only be issued on advice from a microbiologist or ID physician, or under an agreed policy.

- *Use of single dose for surgical prophylaxis.* Prophylactic antimicrobial use has an important part to play in the prevention of postoperative wound infections. However, a key principle is to have a high concentration of the antimicrobial agent(s) in the relevant tissues at the time of the operation, when microbes may contaminate the tissues. For most operations, this requires only a single dose of the antimicrobial(s) at induction of anaesthesia. Only in lengthy operations (i.e. over four hours) may a second intraoperative dose be considered necessary. Policies for the prophylactic use of antimicrobials should state that the single dose is the preferred option.

1.10 Goals and measurable outcomes for antimicrobial stewardship

The AMS team should formulate measurable and defined goals and outcomes. A critical part of testing and implementing changes is the ability to measure them. This allows the team to know whether or not the changes they make are leading to improvements. AMS teams should coordinate the collection and analysis of key metrics to assess achievement of goals, including antimicrobial use, antimicrobial resistance and compliance with antimicrobial policies. Methods for monitoring antimicrobial prescribing and measuring AMS activities are discussed in Chapter 5.

The team should also consider how best to provide feedback to prescribers, other committees and groups, and hospital executive about the program results. As a guide to developing an AMS communication plan, key antimicrobial use should be reported at least quarterly to hospitals, directorates and specific clinical areas. Institutional laboratory susceptibility data should be reported to the same parties at least annually. Unexplained deviation from accepted prescribing practices should be promptly reported back to prescribers. Initially, presenting locally derived, meaningful data to small groups of clinicians (e.g. at departmental meetings) is likely to be more successful than emailing out formal reports; however, a range of strategies is likely to be necessary to disseminate all data. Institution-wide measures of the quality of prescribing should be regularly reported to prescriber groups, and patient safety and quality groups in the organisation.

The team may be able to use existing measurement systems (particularly for costing antimicrobials) or they may have to develop operational definitions for metrics. Similarly, data collection and feedback processes either may exist or need to be developed.

Measurement to support process improvement (in this case, antimicrobial prescribing practice) differs from measurement to evaluate performance or

measurements gathered during research. Improvement measures aim to support bringing new knowledge into daily practice. Data should be collected in many sequential and observable tests, and with a sample size just big enough to learn from and complete further tests. Large blinded tests, controlling for bias and lengthy data collection processes are only appropriate in a research setting, and are unlikely to be practical or successful approaches for routine AMS team use.

The team should plan to collect and plot key measures data over time on a run chart or control chart. A 'balanced' set of measures is ideal and should include:

- *outcome* measures — what is the result? (e.g. restricted antimicrobial consumption, antimicrobial cost, CDI rate)

- *process* measures — are the steps in the process performing as planned? (e.g. compliance with surgical antibiotic prophylaxis prescribing, compliance with restriction conditions)

- *balancing* measures — are the changes causing new problems? (e.g. surgical site infection rate, topical antimicrobial usage, ID consultation rate, mortality due to sepsis).

During the testing and implementing process, frequent small samples are more useful than large infrequent surveys. This will allow the team to see whether changes are resulting in improvement. There are many resources that can be used to design and use measurements for clinical practice improvement, including the *Measurement for Improvement Toolkit* from the Australian Commission on Safety and Quality in Health Care.[a]

Although economic outcomes are not more important than improved clinical outcomes, they are important to measure, especially at the beginning of a new program that is not yet established or funded. A recent review suggested the most likely outcomes associated with AMS programs are cost avoidance, a reduction in antimicrobial resistance rates and a decrease in CDI.[37] Therefore, these are key minimum metrics to consider. This topic is further discussed in Chapter 5.

1.11 Specific antimicrobial stewardship strategies

Each AMS team should determine which AMS strategies are worth testing and how they could be implemented in their local context. These five strategies are considered essential for effective AMS in Australia:

1. Implementing clinical guidelines that are consistent with the latest version of *Therapeutic Guidelines: Antibiotic*[19] and that take local microbiology and antimicrobial susceptibility patterns into account.

2. Establishing formulary restriction and approval systems that include restriction of broad-spectrum and later generation antimicrobials to patients in whom their use is clinically justified.

3. Reviewing antimicrobial prescribing with intervention and direct feedback to the prescriber. (This should, at a minimum, include intensive care patients.)

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a   www.safetyandquality.gov.au/internet/safety/publishing.nsf/Content/CommissionPubs

4. Monitoring performance of antimicrobial prescribing by collecting and reporting unit or ward-specific usage data; auditing antimicrobial use; and using quality use of medicines indicators.

5. Ensuring the clinical microbiology laboratory uses selective reporting of susceptibility testing results that is consistent with hospital or antimicrobial treatment guidelines.

There are also other AMS activities that have been shown to be effective. We suggest that these are implemented according to local priorities and resources:

1. Educating prescribers, pharmacists and nurses about good antimicrobial prescribing practice and antimicrobial resistance.

2. Using point-of-care interventions including streamlining or de-escalation of therapy, dose optimisation or parenteral-to-oral conversion.

3. Using information technology such as electronic prescribing with clinical decision-support or online approval systems.

4. Publishing facility-specific antimicrobial susceptibility data annually.

Selected AMS strategies are briefly described in the following subsections with details included in subsequent chapters of this book.

1.11.1 Prescribing guidelines

Prescribing guidelines for antimicrobials are an essential component of AMS programs. Hospitals should have prescribing guidelines for treatment and prophylaxis for common infections relevant to the patient population, the local antimicrobial resistance profile and the surgical procedures performed in the institution. The *Therapeutic Guidelines: Antibiotic*[19] are recognised as a national standard for antimicrobial prescribing in Australia.[2] Institutional clinical guidelines developed for local use should accord with these guidelines. Guidance for switching from intravenous to oral therapy should also be available. The development and implementation of guidelines is discussed in more detail in Chapter 8.

The SACAR suggested list of 'regimens' serves as a guide to common clinical syndromes appropriate for local antimicrobial prescribing guidelines (see Box 3).

As a minimum, guidelines should be available for:

• common clinical scenarios

    » community acquired pneumonia

    » hospital acquired pneumonia

    » urinary tract infection

    » skin and soft tissue infection

    » intra-abdominal infection

    » bloodstream infections

    » sepsis

- empirical use (all hospitals should specify use of *Therapeutic Guidelines: Antibiotic*[19] for guidance on empirical use)
- surgical prophylaxis
- intravenous-to-oral antimicrobial switch.

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Box 3   United Kingdom Specialist Advisory Committee on Antimicrobial Resistance recommended guidelines

Treatment of:

- urinary tract infections
- upper respiratory tract infections
- lower respiratory tract infections, including community and hospital acquired pneumonia, and exacerbations of chronic obstructive pulmonary disease
- soft tissue infections, including injuries or bites, cellulitis, chronic ulcers and necrotising fasciitis
- central nervous system infections, including bacterial meningitis, viral encephalitis
- gastrointestinal infections such as food poisoning and intra-abdominal sepsis
- genital tract infections
- bloodstream infections
- eye, ear, nose and throat infections
- sepsis of unknown origin
- specific confirmed infections; for example, treatment regimens for methicillin-resistant *Staphylococcus aureus*, *Clostridium difficile* and tuberculosis
- endocarditis.

Prophylaxis use for:

- prevention of bacterial endocarditis (procedure-specific criteria should be agreed upon to identify which patients should receive prophylaxis)
- endoscopic procedures (details should be given of which individuals, considered at high risk, should receive prophylaxis; for example, neutropenic patients)
- surgical procedures (recommendations should be made for all common surgical interventions, including timing of initial dose and exceptional circumstances for repeat doses)
- splenectomy patients (provide details of both the immunisation and antimicrobial prophylaxis requirements).

Source: Specialist Advisory Committee on Antimicrobial Resistance (SACAR) Antimicrobial Framework[36]

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See Chapters 6 and 8 for further information on guideline development and implementation. Examples of guidelines used in Australian hospitals are provided in Appendix 2.

1.11.2 Core antimicrobial stewardship interventions

The two core AMS strategies (formulary restriction and approval systems, or review with intervention and feedback) are described in Chapters 2 and 3. Table 1.1 compares key characteristics of these two approaches. They should be considered complementary and are both recommended as essential AMS elements.

An information technology system that supports these strategies is ideal, but there are many examples of effective AMS programs that have not had this advantage initially and that have been very successful.

1.11.3 Antimicrobial stewardship 'care bundles'

'Care bundles' are increasingly used in healthcare quality improvement as a structured way of improving the processes of care and patient outcomes. A bundle is a small, straightforward set of three to five evidence-based practices that, when performed collectively and reliably, have been proven to improve patient outcomes.[38]

Cooke and Holmes[39] propose the use of care bundles to improve appropriate antimicrobial prescribing in acute care and surgical prophylaxis. Inherent in the approach is a goal of engaging specific clinical teams (e.g. individual medical or surgical units). The approach they describe combines routine compliance monitoring and feedback, combining essential AMS strategies 1, 3 and 4 (Section 1.11). The two bundles ('treatment' and 'surgical prophylaxis') could be implemented separately or in combination, and AMS teams could adapt the focus of the proposed bundles to their local context.

Treatment bundle

The Cooke and Holmes treatment bundle[39] is divided into measurable practices that the authors suggest should take place at both initiation and at continuation of treatment. In this approach, compliance with these elements is monitored and used as targets for improved practice.

At initiation of treatment, the prescriber should:

- provide a clinical rationale for antimicrobial initiation

- send the appropriate specimens to a diagnostic microbiology laboratory (according to local policy)

- select the antimicrobial according to local policy and having considered the patient risk group (including their drug allergy profile)

- consider removal of any foreign body, drainage of pus or other surgical intervention, as appropriate.

Table 1.1   Comparison of core antimicrobial stewardship interventions

	Formulary restriction and approval systems	Review with intervention and feedback
Principles of intervention	Mandatory, requires: • action by prescribers to seek approval to prescribe • resources to support the approval process	Recommendations made after prescribing

Timing of intervention	Effect only at point of prescription (i.e. only initial choice and dose)	Intervenes after antimicrobial prescribing, when there is greater opportunity for effect
		Review may be:
		• *prospective*, with direct feedback provided to the clinician before the drug is dispensed. This requires antimicrobial restrictions and pre-authorisation systems to be in place. It provides an opportunity for additional education as well as feedback on the episode of care
		• *retrospective*, after therapy has been initiated. Examples of retrospective recommendations include
		  » discontinuing therapy after 2–3 days where no infective cause is found
		  » changing from broad spectrum to narrow spectrum based on results
		  » switching from parenteral to oral therapy

Scope of intervention	Scope limited to what is on restricted list	Can adjust to resources available (e.g. twice weekly retrospective review) or target to needs or priorities (e.g. notifying pharmacy or biochemistry laboratory if gentamicin is used) As a minimum, prospective review and feedback should be provided for intensive care patients
Cost of intervention	Cheaper to implement if use computerised or phone approval (but 24-hour coverage is necessary)	Time required by clinician and pharmacist to provide follow up The retrospective approach is likely to be less resource-intensive, but may be less effective overall
Possible risks of intervention	Can delay administration if prior approval required	

During continuation of treatment, there should be:

- daily consideration of de-escalation, intravenous–oral switch or stopping antimicrobials (based on clinical picture and laboratory results)
- monitoring of antimicrobial drug levels, as required by local policy.

Routinely measuring compliance with these six processes provides a measure of how well treatment policy is being adhered to, and directs attention for AMS team activity.

Surgical prophylaxis bundle

The proposed bundle[39] is similar to that used in other surgical safety quality improvement programs and includes:

- selecting antimicrobials that match local guidelines (having considered patient allergies)
- timing the first dose to be 30–60 minutes pre-incision
- stopping antimicrobial administration within 24 hours after the pre-operative dose or the first dose after the operation.

Routinely measuring compliance with these three processes provides a measure of how well surgical prophylaxis policy is being adhered to, and directs attention for AMS team activity.

Hospitals using the care bundle approach to antimicrobial prescribing should develop systems to monitor compliance with the above practices in appropriate patient groups and provide regular feedback to prescribers. This could improve local prescribing of antimicrobials and provide ready access to process measures as quality improvement indicators. This may be a particularly attractive strategy for sites that could incorporate this into existing quality improvement infrastructure, or for smaller sites with limited AMS team resources that could use clinical teams to take ownership of the improvement work.

1.11.4 Other antimicrobial stewardship strategies

Other activities that are complementary to those outlined above that should be considered for inclusion in an AMS program are: education of prescribers, pharmacists and nurses; point-of-care interventions (such as streamlining or de-escalation of therapy, dose optimisation, and parenteral-to-oral conversion, often provided as part of prospective review and feedback strategy); the use of information technology (such as electronic prescribing with clinical decision-support or online approval systems); and annual publication of facility-specific antimicrobial susceptibility data.

1.11.5 Selecting antimicrobial stewardship strategies to test

Although we regard the strategies listed above as necessary elements of any AMS program, there is not one single AMS model that will deliver optimal antimicrobial prescribing in every context. In addition to selecting the strategies that have the best efficacy, the AMS team needs to consider which strategies are most likely to be successful in their specific context and how best to implement them. When making this decision, teams should consider attributes of changes that are more likely to be successfully spread and sustained in an organisation. Evidence from the work of Everett Rogers[40] suggests that there are five attributes of 'worthy' ideas to consider for testing and implementation:

*   relative advantage over the status quo or alternative ideas

*   compatibility with existing values, experiences and needs

*   relative simplicity (as complexity can inhibit an adopter's ability to understand and use the ideas)

*   ability to trial the idea locally, allowing ideas to be tested on a small scale and reversed if desired

*   ability to observe the ideas in practice.

The information gathered during the readiness assessment (described in Section 1.8) could be used to determine the strategies to be tested and considered for implementation.

A program demonstrating some success in the short term (i.e. 'quick wins') is more likely to be well regarded, and gain acceptance and support. The major short-term benefits of AMS are overall cost savings and, if existing infrastructure and resources are very limited, AMS teams may want to start with targeting specific high-cost drugs that have suboptimal local use. Pharmacy costing data, comparative-use rates or a baseline audit of the appropriateness of antimicrobial use will provide a guide to local priorities. Common examples of such high-cost drugs are IV quinolones, carbapenems (such as meropenem) and aztreonam. Third-generation cephalosporins are another important target group, but demonstrable cost savings for this drug class may be less. Other low-cost but high-risk agents (e.g. aminoglycosides) can be included for safety reasons. Patients that receive these agents can be reviewed with feedback to prescribers providing an opportunity to intervene in a timely and ongoing manner. The review can be used to provide education and to gather additional information about intended versus actual use to demonstrate savings and improvement.

An example of a successful AMS program that uses such a strategy is described in Box 4.

Box 4   An example of a successful Australian antimicrobial stewardship (AMS) program

Context for AMS program

- 800-bed, metropolitan teaching hospital

- an existing restricted formulary that required prior approval from a microbiologist or an infectious diseases (ID) physician to use selected antimicrobials

- an existing drug and therapeutics committee, drug use and audit group, and an infection control committee

- existing data (collected as part of an international collaborative study) demonstrating high antibiotic use rates; cost of antimicrobials steadily increasing each year; recent outbreaks of vancomycin-resistant *Enterococcus* and methicillin-resistant *Staphylococcus aureus*; and previous surveys of surgical antibiotic prophylaxis showing suboptimal compliance

- a history of difficulty in introducing and supporting clinical information technology systems

- some local clinical guidelines developed and promoted, widespread availability of *Therapeutic Guidelines: Antibiotic*[19]

- book and electronic resources

- a clinical pharmacist on staff with overseas experience in AMS.

The team

A team for AMS implementation was proposed:

- The hospital executive was presented with evidence of suboptimal antimicrobial use and high cost. This lead to a request to appoint a clinical pharmacist 2.5 days a week for six months to work with a nominated ID physician to lead an AMS program with continuation contingent on proof of savings.

- An AMS committee was formed and reported to the drug and therapeutics committee. The committee comprised an ID physician (nominated by the committee as chair), an ID pharmacist (secretary) and representatives from the infection control, drug use and assessment group; a hospital executive; and two more physicians (an intensivist and a nephrologist).

Box 4   An example of a successful Australian antimicrobial stewardship (AMS) program *continued*

The strategies

The strategies developed to implement the AMS program included:

- *restrictive strategies*
    - » continuing to use the restricted antimicrobial formulary
    - » using a locally designed Microsoft Access database to directly enter details of patients for whom permission has been given for prescription of key restricted antibiotics (carbapenems, intravenous quinolones, vancomycin, and third or fourth-generation cephalosporins)
    - » notifying the ID pharmacist of patients receiving restricted antibiotics
    - » generating a list 3–5 days each week of all patients receiving restricted agents to be seen on the AMS round (list generated by the ID pharmacist)
- *review and feedback*
    - » commencing AMS rounds as a means of prospective review, intervention and feedback
    - » reviewing the clinical notes, results of microbiology and other investigations of patients on restricted antimicrobials (aiming to review within two days of start date) and recommending (in writing) in the integrated notes or by direct phone call to the treating doctor (to be done by the ID physician and pharmacist)
- *prescribing guidelines*
    - » developing more local clinical treatment and management guidelines
- *monitoring performance of the AMS program*
    - » auditing compliance with community acquired pneumonia protocol, surgical antibiotic prophylaxis and gentamicin use
    - » participating in the National Antimicrobial Utilisation Surveillance Program (NAUSP) to monitor antimicrobial use
- *other strategies*
    - » promoting further antimicrobial prescribing education
    - » lobbying for the microbiology laboratory to provide local antibiogram data
    - » investigating the introduction of a computerised decision-support program.

Box 4   An example of a successful Australian antimicrobial stewardship (AMS) program *continued*

Results of the AMS program

- In the first six months of the AMS round in 2005, 273 patients were reviewed and 87% of the recommendations made were followed, resulting in estimated savings of $85 000. Only one complaint from a prescriber has been received in the four years of the AMS program, during which time the antimicrobial treatment of over 2000 patients has been reviewed.

- The success of the program and demonstrated cost savings resulted in the creation of a permanent full-time position for an ID pharmacist. This increased capacity allowed the program to expand to include an ongoing intravenous–oral switch campaign, the development of a number of clinical guidelines, increased compliance auditing, and improved prescriber and pharmacist education.

- Thus far, any attempts to introduce computerised decision support have been unsuccessful.

- The round has provided a dynamic and efficient mechanism to respond to emerging issues. For example, as a result of concerns about adverse events from aminoglycoside use, patients receiving more than four days of aminoglycosides were added to the AMS round, as were all inpatients with *Staphylococcus aureus* infection.

The size and elements of an AMS program will need to be scaled to meet hospital requirements and resources. The program should also be expected to evolve over time, depending on the results of testing, evaluation and ongoing monitoring of key metrics. A principal referral hospital will benefit from a comprehensive program with multiple strategies supported by a pharmacist (ideally with ID training), and an ID physician or clinical microbiologist.[15] Smaller hospitals, with few resources, may need to prioritise their activities, but can still effect cost savings and improved use of antimicrobials. LaRocco described an AMS team led by an ID physician (8–12 hours per week) and a clinical pharmacist performing review and feedback in a 120-bed nonteaching hospital, effecting a 19% reduction in antimicrobial costs.[41]

Some examples of the types of strategies employed in successful AMS programs overseas and in Australia are provided in Table 1.2. Other examples of outcomes of Australian AMS programs are provided in Appendix 1.

Table 1.2   Examples of strategies employed in successful antimicrobial stewardship programs

Country	Size of hospital	Strategy
United States[15]	Large teaching hospital	Goals in the first year were to: • create a formulary pocket guide • begin prospective review with feedback and intervention • optimise dosing • reduce unnecessary combination therapy • switch from IV to oral therapy.
United States[42]	Medium-sized community hospital	Prospective review with feedback on: • discontinuing therapy after 2–3 days where no infective cause found • changing from broad spectrum to narrow spectrum based on results • switching from IV to oral therapy Pharmacy Committee-based formulary management Automatic stop orders after 7 days Limited reporting of susceptibility testing Ongoing education programs for residents and staff physicians Exclusion of pharmaceutical industry representative detailing antimicrobials in the hospital
United States[14]	Large teaching hospital	Guidelines for antimicrobial treatment and prophylaxis Establishing appropriate dosing and dosage intervals Restriction and prior approval systems Evaluation of agents for addition or deletion to formulary Streamlining therapy Ongoing education initiatives Continuous monitoring of antimicrobial use
Australia[25]	Large, tertiary teaching hospital	Local antimicrobial guidelines with clinical teams engaged in development and implementation Online registration (approval) system for broad-spectrum agents Twice-weekly ID and microbiology rounds in ICU Regular targeted drug usage evaluations and audits of antimicrobial use, clinical syndromes or surgical prophylaxis with feedback to clinicians Use of data contributed to the National Antimicrobial Utilisation Surveillance Program to monitor use and benchmark against similar hospitals

ICU = intensive care unit; ID = infectious diseases; IV = intravenous

1.12 Testing antimicrobial stewardship strategies

Testing in quality improvement work allows unforeseen problems to be resolved, and interventions to be evaluated and refined before full implementation into widespread day-to-day operations. In general, testing should follow a sequence of Plan-Do-Study-Act (PDSA) cycles. Each sequence should increase in scope and scale, and be analysed, allowing subsequent tests to be refined.[27-28]

For example, a hospital AMS team decides to introduce a restricted antimicrobial formulary, with required prior phone approval from an ID physician before selected agents are dispensed. They would be wise to initially test the approval and dispensing process in a range of conditions. For example, they could work with one cooperative prescriber to see if the process works well at different times of the day, on weekends, and when different dispensing pharmacists or ID physicians are on duty. After making any necessary refinements, the team could then plan on including all respiratory patients, then all medical patients and so on.

1.13 Implementing and sustaining successful antimicrobial stewardship programs

Once changes have been developed and tested, it is time to implement the changes on the basis of what was learned. Implementing complex broad-scale changes, such as AMS strategies, is challenging and will benefit from careful planning, providing support during and after implementation, and recognising and addressing social aspects of change.

An implementation plan should consider approaches to standardisation, training, and ongoing measurement and feedback. These elements all support making changes that are permanent in an organisation.[27]

The social aspects of change should not be underestimated — AMS interventions may be perceived differently by different healthcare professionals. For example, introducing a prior approval system could be perceived as restricting prescriber autonomy, adding work to ID physicians or placing pharmacists in a position of potential confrontation if asked to enforce restrictions. Resistance to change can be minimised by communicating why change is required, providing information on how the change will occur, and reporting ongoing progress to affected individuals and groups. Incorporating a range of individuals and perspectives in the planning and testing phase will also be helpful.[27]

An example of an organisation's approach to implement a stewardship program is provided in Table 1.3. The plan was developed by staff at the North Coast Area Health Service in New South Wales (a regional health service comprising 18 hospitals).

Table 1.3   North Coast Area Health Service culture change initiatives

Priority 1: General	Priority 2: Staffing	Priority 3: Stakeholders	Priority 4: Resources	Priority 5: Education, awareness and involvement	Priority 6: Ongoing management	Priority 7: Future spending
Advocate prescriber compliance with the MINDME philosophy, as recommended by NSW Health through email and poster placement in all wards and pharmacies **M** microbiology guides therapy **I** indications should be evidence based **N** narrowest spectrum required **D** dosage appropriate to the site and type of infection **M** minimise duration of therapy **E** ensure monotherapy in most cases	Ensure optimal pharmacy staffing Remove ceftriaxone from ward stock Provide training in ID for one clinical pharmacist from each B2 hospital Develop a program of parenteral-to-oral antibiotic prescribing Provide feedback to prescribers via antibiograms Commence recording antimicrobial consumption rates Conduct regular drug use studies and regular AHS antimicrobial audits Ensure optimal infection control staffing Employ an AHS ID physician or clinical microbiologist (ideally, an ID physician at each B2 hospital)	Engage AHS DTC to make appropriate antimicrobial prescribing a priority. AHS DTC to draft an area antimicrobial prescribing policy that includes: • (initial) empowering clinical pharmacists with ID training to change certain antimicrobials from parenteral-to-oral administration • (initial) specifying antimicrobials that require monitoring • (initial) developing and supporting AMS programs at each B2 hospital • (ongoing) monitoring compliance with area policy; assessing effectiveness of interventions with regular audit • (ongoing) reviewing specified antimicrobials that require annual monitoring to reflect antibiogram trends	Regularly remind prescribers that the most recent version of the Therapeutic Guidelines: Antibiotic can be accessed through the intranet of every ward of the B2 hospitals Engage the National Prescribing Service to provide education and quality assurance programs Engage the NSW TAG to share resources regarding strategies to improve antimicrobial prescribing Use AMS development guidelines outlined by IDSA and SHEA to tailor area-wide programs	Recruit respected educators (i.e. clinical pharmacists, ID physicians) Increase prescriber awareness through education about the benefits of judicious antimicrobial prescribing and the serious consequences of inappropriate prescribing Invite prescribers to provide input into the development of AMS programs prior to implementation to promote ownership through involvement Cultivate opinion leaders (if there is no ID physician at each site, administrators need to engage medical staff to find opinion leaders willing to drive change)	Continue to improve infection control processes to reduce the spread of multiresistant organisms by ensuring compliance with NSW Health strategies to reduce HAIs	Invest in rapid diagnostic testing for multiresistant organisms as this will allow more rapid intervention of infection control measures to prevent secondary spread

AHS = Area Health Service; AMS = antimicrobial stewardship; B2 = large regional and remote hospitals; DTC = drug and therapeutics committee; HAI = healthcare associated infection; ID = infectious diseases; IDSA = Infectious Diseases Society of America; NSW = New South Wales; NSW TAG = NSW Therapeutic Advisory Group; SHEA = Society for Healthcare Epidemiology of America

Source: Howell E. Antibiotic audit report. North Coast Area Health Service, NSW 2009.

1.14 Summarising requirements for antimicrobial stewardship programs

The elements of hospital AMS programs are well described in the literature and have been used to formulate the key recommendations of this chapter.[1, 12, 15-17] Minimum AMS measures have been developed,[16] and evidence-based guidelines[1] and recommendations for good antimicrobial practice in hospitals published.[17-18] The most comprehensive guidelines for developing a hospital AMS program have been published by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America.[1]

This work, along with the evidence from the Cochrane Collaboration review of interventions for improving antimicrobial prescribing practice in hospitals[22] has been used to develop requirements for AMS programs in Australian hospitals, summarised in Box 5.

Box 5   Requirements for antimicrobial stewardship programs

Structure and governance

The overall accountability for antimicrobial management control lies with the hospital administration. They are responsible for ensuring an antimicrobial management program is developed and implemented, and outcomes are evaluated.

Hospital management support is needed, including:

- providing dedicated resources for stewardship activities, education, and measuring and monitoring antimicrobial use

- establishing a multidisciplinary antimicrobial stewardship (AMS) team with core membership (wherever possible) of either an infectious diseases physician, clinical microbiologist or nominated clinician (lead doctor), and a clinical pharmacist

- ensuring that AMS resides within the hospital's quality improvement and patient safety governance structure, and clear lines of accountability exist between the chief executive; clinical governance; drug and therapeutics, and infection prevention and control committees; and the AMS team.

Box 5 Requirements for antimicrobial stewardship programs
continued

Essential strategies for all hospitals

The following five strategies are considered essential for effective AMS in Australia:

- implementing clinical guidelines that are consistent with the latest version of *Therapeutic Guidelines: Antibiotic*,[19] and which take into account local microbiology and antimicrobial susceptibility patterns

- establishing formulary restriction and approval systems that include restricting broad-spectrum and later generation antimicrobials to patients in whom their use is clinically justified

- reviewing antimicrobial prescribing with intervention and direct feedback to the prescriber — this should, at a minimum, include intensive care patients

- monitoring performance of antimicrobial prescribing by collecting and reporting unit or ward-specific use data, auditing antimicrobial use, and using quality use of medicines indicators

- ensuring the clinical microbiology laboratory uses selective reporting of susceptibility testing results that is consistent with hospital antimicrobial treatment guidelines.

Antimicrobial stewardship activities according to local priorities and resources

The following activities may be undertaken according to local priorities and available resources:

- educating prescribers, pharmacists and nurses about good antimicrobial prescribing practice and antimicrobial resistance

- using point-of-care interventions, including streamlining or de-escalation of therapy, dose optimisation, or parenteral-to-oral conversion

- using information technology such as electronic prescribing with clinical decision-support or online approval systems

- annually publishing facility-specific antimicrobial susceptibility data.

2 Formularies and antimicrobial approval systems

Author: Kirsty Buising

2.1 Key points

- Formularies can be used to influence patterns of antimicrobial use in hospitals. Each hospital should have a formulary for antimicrobial drugs, and the drug and therapeutics committee of the hospital should define rules that restrict access to particular antimicrobial agents.

- Restrictions on the use of antimicrobials have played an important role in aborting outbreaks of resistant bacteria.

- Antimicrobial approval systems have been shown to be effective in optimising antimicrobial use in a hospital setting — their use has been associated with reduced volumes of drugs used, reduced drug costs, fewer adverse drug reactions and shorter lengths of stay.

- Approval systems may be used for preprescription or postprescription approval.

- Experts providing the approval should be members of the antimicrobial stewardship teams or their nominees.

- Computerised systems have been found to be acceptable to clinicians as a means of facilitating antimicrobial approvals in hospitals.

2.2 Recommendations

2.2.1 Hospitals have a list of restricted antimicrobial agents and criteria for their use which is consistent with *Therapeutic Guidelines: Antibiotic.*[19]

2.2.2 Hospitals implement an antimicrobial approval system.

2.2.3 Compliance with the approval process is audited on a regular basis.

2.2.4 Expert advice is available 24 hours a day to guide clinicians in prescribing antimicrobials.

2.3 Strategies for antimicrobial stewardship

Strategies for antimicrobial stewardship (AMS) fall into 'educative' strategies, where prescribers are provided with guidelines and taught how to select antimicrobial agents more appropriately, and 'restrictive' strategies, in which prescribers are prevented from accessing particular antimicrobial agents unless criteria are met and formal approval is granted by a nominated person. Approval may be required preprescription, or postprescription within a specified time period (e.g. 48 hours).

Several leading guidelines on AMS endorse the use of both educative and restrictive strategies to facilitate comprehensive stewardship in hospital settings. This chapter will focus on describing different restrictive strategies for AMS.

Some authors have suggested that restrictive strategies have the greatest impact on prescribing behaviour. Dellit et al. in the Infectious Diseases Society of America and Society of Healthcare Epidemiology of America guidelines,[1] and MacDougall and Polk in their comprehensive review,[12] all recommend that antimicrobial restriction and specifically antimicrobial approval systems have a central place in any AMS program for hospitals.

The use of antimicrobial formulary and approval (pre-authorisation) systems to influence appropriate antimicrobial prescribing are described below. The roles of the different departments in supporting these restrictive strategies are further described in Chapters 7, 8 and 9. See Appendix 2, Section A2.1 for examples of restricted antimicrobial policies and guidelines from Australian hospitals.

2.4 Formulary systems

In its simplest form, a formulary is a list of drugs, including antimicrobial agents, that has been approved for use in a hospital. However, formulary systems can also be used to influence prescribing behaviour by restricting access to particular drugs and by applying rules governing drug use. A formulary that includes a list of restricted antimicrobials is an essential component of an AMS program.[1, 12, 16-17, 20]

The antimicrobial formulary should be appropriate to the needs of the hospital and should take into account the range of antimicrobials required, the clinical orientation of the hospital and local antimicrobial resistance. It should be updated periodically and compliance with it audited.[17, 20]

The responsibility for creating and maintaining a drug formulary usually lies with a hospital's drug and therapeutics committee. The role of this committee is to evaluate the evidence regarding the efficacy, safety and cost of new agents before deciding whether to endorse their use in the hospital and list them on the formulary. The drug and therapeutics committee may have an antimicrobial subcommittee or may use the AMS team to evaluate requests for new antimicrobial agents or new indications for use, and to make recommendations for formulary listing.

In many circumstances, formulary decisions may have criteria attached to the approval for use of a drug in the hospital (e.g. use is approved only for a particular unit, for patients with a particular condition, or where other options are contraindicated due to intolerance or demonstrated failure). In the case of antimicrobial agents, certain drugs may be restricted for use only with approval by nominated expert prescribers (e.g. infectious diseases [ID] specialists or microbiologists).

It is important that antimicrobial formulary decisions are informed by local microbiologic information. If, for example, resistance to one antibiotic class has been emerging in local bacteria, then the drug and therapeutics committee may respond by directing prescribing towards alternative agents. This may require a change in criteria for approval to use the alternate agents. It is therefore important for microbiologists and ID physicians to provide continuous expert advice to drug and therapeutics committees (by membership of the committee or liaison with the AMS team).

2.4.1 The evidence for restricted formularies influencing antimicrobial prescribing

It has been well demonstrated that formularies dictate prescribing patterns in hospitals and direct prescribing away from some drug classes and towards others. This clearly affects drug consumption patterns and expenditure. For example, Aspinall et al.[43] compared 15 hospitals in the United States, where 12 had free access to fluoroquinolones and 3 had restricted access as indicated in their respective hospital formulary. The study sampled 200 cases of acute respiratory infection presenting to each hospital and found that 17% of patients were treated with fluoroquinolones for respiratory tract infections at the unrestricted hospitals compared with just 6% at the hospitals with a formulary. Multivariate analysis of the factors that predicted the use of fluoroquinolones found that hospital site was strongly predictive and the study concluded that a formulary can have an important impact on prescribing practices. In turn, prescribing practices may have an impact on the local prevalence of some resistant pathogens.

Few published studies have directly examined the use of formularies to guide antimicrobial prescribing with the primary aim of tackling antimicrobial resistance. Studies that do address antimicrobial resistance usually incorporate some form of restriction of one class of drug, followed by an addition of another class to the formulary in an effort to 'replace' the first class. Such changes in formularies have been shown to be associated with changes in local rates of some antibiotic-resistant pathogens, but the authors tend to attribute the observed changes to the formulary switch by virtue of an association in time only. Unfortunately, most of these studies have occurred over short time periods and at single centres — studies run over longer time periods and at multiple centres would be preferable to better explore this complex association. Some examples of the studies are reported in Table 2.1.

Table 2.1   Effect of formulary changes on prevalence of multiresistant pathogens

Author	No. of sites	Description of intervention	Results
Landman et al. (1999)[44]	One hospital in the United States	Restriction on use of third and fourth-generation cephalosporins, clindamycin and vancomycin; approval required for their use. Beta-lactam–beta-lactamase combinations (piperacillin–tazobactam and ampicillin–sulbactam) were simultaneously added to the formulary without requirement for approval.	There was a shift in prescribing behaviour away from cephalosporin-based therapy and towards extended spectrum penicillin use. Concurrently, there were reductions in the rates of methicillin-resistant *Staphylococcus aureus* (MRSA), and ceftazidime-resistant *Klebsiella*, which the authors hypothesised were attributable to the change in prescribing patterns.
Walbrown et al. (2008)[45]	10 veterans' affairs hospitals in the United States	A formulary change from levofloxacin to gatifloxacin with 12-month data collection, 6 months pre and postintervention.	A rise in *Clostridium difficile* infection (CDI) was noted, from 2.3 cases per 1000 antibiotic days (54% associated with previous fluoroquinolone use) to 3.4 cases per 1000 antibiotic days (67% associated with previous fluoroquinolone use). The study concluded that the formulary does dictate prescribing patterns and that different drugs within a class may have different effects on CDI rates.

Table 2.1   **Effect of formulary changes on prevalence of multiresistant pathogens** *continued*

Author	No. of sites	Description of intervention	Results
Winston et al. (2004)[47]	One hospital in the United States	Formulary change from ticarcillin-clavulanate to piperacillin-tazobactam. Active surveillance of all patients at admission and discharge from the intensive care unit was undertaken.	There was a reduction in the vancomycin-resistant *Enterococcus* (VRE) acquisition rate (11.5% versus 7.6%, relative risk 0.68, $P = 0.07$) and a fall in clinical VRE isolates (0.58 per 1000 bed-days pre to 0.33 per 1000 bed-days post) with the change in formulary. The authors of this study proposed that the change in prescribing behaviour caused by the formulary switch led to the change in VRE rates.

In summary, the evidence supports the inclusion of a formulary system in hospital AMS programs, with a list of restricted antimicrobial agents and criteria for their use. Examples of restricted formularies are provided in Appendix 2, Section A2.1.

2.5   Antimicrobial approval systems

The use of a restricted formulary and an approval system, which facilitates restriction of broad-spectrum antimicrobials to patients where use is clinically justified, are considered essential requirements of any antimicrobial stewardship program.[1, 12, 16]

A formulary describes the agreed indications for use of particular antimicrobial agents and an approval system provides a mechanism through which the formulary restrictions can practically be enforced.

2.5.1   The evidence for antimicrobial approval systems

Several studies suggest that antimicrobial approval systems can reduce the volume of broad-spectrum antimicrobials prescribed, thereby reducing drug expenditure.[48-51] A reduction in adverse drug reactions for patients has also been described.[48, 52] Effects on patient outcomes are less well described, although reduced lengths of hospital stay have been reported after the deployment of an antimicrobial approval system, as has the use of more appropriate empirical antimicrobial therapy.[52]

Studies on the effectiveness of restrictive antimicrobial strategies in addressing the problem of antimicrobial resistance have generally been related to limiting the use

of a specific antimicrobial class to tackle an outbreak of a specific pathogen. For example, restricting:

- cephalosporins and vancomycin to deal with vancomycin-resistant *Enterococcus* (VRE)[53]

- cephalosporins to tackle an outbreak of *Acinetobacter*[50] or resistant *Klebsiella*[54] or resistant *Enterobacter* and *Pseudomonas*[55]

- cephalosporins to address outbreaks of *Clostridium difficile*.[41-42, 56-57]

Formulary restriction and preauthorization requirements can lead to immediate and significant reductions in antimicrobial use and cost.[1]

The effect of restricting a large number of antimicrobials on the endemic resistance profiles of several different bacterial pathogens has been described in some single-site studies. Paterson reported anecdotal evidence of an improvement in sensitivity patterns in local bacteria with the introduction of a restrictive stewardship system.[29] Martin and Ofotokun[58] showed that an antimicrobial control policy that reduced cephalosporin, vancomycin and carbapenem use led to a reduction in multidrug-resistant gram-negative pathogens. Cook et al.[59] described no change in the antibiogram for gram-negative bacilli before and after an AMS program, but these data were only collected for a relatively short time period (two years either side).

In general, the effects of restrictive systems addressing multiple antibiotics on endemic antimicrobial resistance patterns of multiple bacteria over long time periods has not been widely reported. The relationship is likely to be complex, and more work is needed in this field.

2.5.2 Mechanisms for administering approval systems

The practical mechanisms for administering approval systems have varied, but basically some form of approval must be granted by an expert prescriber under a system that fits the workflow of the organisation. Preprescription approval may be by telephone or by filling in a drug order form. An example of a drug order form is provided in Section A2.1 in Appendix 2. Bamberger and Dahl[55] described a system where written justification for the use of ceftriaxone or ceftazidime had to be submitted to the pharmacy before the drugs could be used. McGowan and Finland[48] described a system that required prescribers to telephone the ID consultant to discuss a case before approval. Until recently, telephone approval has been the predominant method used by many Australian hospitals.

However, these methods have a number of drawbacks:

- Telephone approval can be onerous for staff who must be available to grant approval as it is required — they therefore receive continual interruptions.

- The advice provided may be inconsistent if different experts rotate the role.

- It can be difficult to keep a record of the advice given and to communicate the advice to others involved in a patient's care, including pharmacy staff supplying the drug.

Postprescription approval systems usually entail a review of a patient prescribed a restricted drug by an expert prescriber within a given time period.[60] Reviews may be carried out in some settings by a dedicated AMS team, including ID physicians, a microbiologist, and pharmacists who perform daily ward rounds. Such systems can be very successful as they provide individualised advice and direct interaction with prescribers face to face. The main difficulty with postprescription approval systems is that large resources are required to maintain them. In addition, communication advice usually needs to occur via the medical record and auditing can be difficult.

Some articles describe a mix of different strategies. In a study from Hong Kong, prescribers were required to fill in an antibiotic order form if they wanted to use one of 12 restricted antimicrobials beyond one day. Receipt of a form prompted review by an ID specialist and concurrent feedback was provided (i.e. a combination of preprescription approval and postprescription review).[61] Woodward et al.[49] described a multitiered system whereby some agents required preprescription approval before access was allowed, while other drugs could be used without preprescription approvals, but triggered an automatic postprescription review at 72 hours.

Restrictive strategies require close collaboration with pharmacy, clinical microbiology and ID staff to be successful.[1, 16] Approval systems have been shown to be cost-effective, even personnel-intensive systems. For example, in a study from Hong Kong that used an AMS team with a mix of pre and postprescription approvals, an economic analysis demonstrated an overall cost saving, if AMS program personnel costs (US$71 000 per year) were weighed against antibiotic costs (US$380 000 per year).[61]

Some examples of antimicrobial approval systems are provided in Appendix 2, Section A2.1.

2.5.3   Automated approval systems

The practical implications of restricting large numbers of antimicrobials can be quite significant for hospitals. Personnel requirements (resources and time) can become onerous with telephone approval systems or an AMS team, because approvals may be required at any time of the day. This can lead to delays and frustration for both the prescriber and the authorised approver. Automation using computerised antimicrobial approval systems is a possible solution to this problem. Electronic approval systems for individual antimicrobial agents have been described in several centres.[62-63] Both Richards et al.[64] and Grayson et al.[65] describe clinical electronic advice and approval systems introduced into Australian teaching hospitals that have significantly reduced the burden of a wholly telephone-based approval system for third-generation cephalosporin use.

Recently, electronic systems to manage larger numbers of antimicrobials have been reported. Some of these systems are large, institution-specific decision-support systems that trigger alerts for particular drugs and make recommendations, rather than restricting access to drugs. These have been successfully implemented at some major sites in the United States and are further described in Chapter 10.

A transferable web-based electronic antimicrobial approval system (Guidance DS), which covers several restricted antimicrobials, has had good uptake in Australia, leading to reduced drug consumption, improved resistance patterns in some gram-negative isolates in the intensive care unit and acceptable usability for clinicians. The system has been used to restrict the use of third and fourth-generation cephalosporins, carbapenems, extended-spectrum penicillins, aminoglycosides, fluoroquinolones and glycopeptides. Buising et al.[66] evaluated trends in antimicrobial consumption for five years before the deployment of the system, and compared this with the patterns observed over two years after implementation in one Australian tertiary hospital. Reductions in the use of all classes of broad-spectrum antibiotics were observed, with the exception of extended-spectrum penicillins, as increased use was prompted by a change in hospital protocols for febrile neutropenia. The system was incorporated successfully into clinicians' workflow, with between 200 and 250 uses per month in a 350-bed hospital.

An independent evaluation of the Guidance DS system demonstrated that clinicians and pharmacists found it easy to use and incorporate into their workflow.[67] The reduced consumption of broad-spectrum antimicrobials was associated with a subsequent fall in multiresistant gram-negative bacteria in the intensive care unit over time. There was no negative impact on patient outcome (no increase in patient deaths or lengths of stay for gram-negative bacteraemia, despite the access limits to broad-spectrum antimicrobials). The Guidance DS system has been successfully transferred to other hospitals in Victoria and Tasmania, and the effect on prescribing in these sites will be the subject of ongoing study.

2.5.4   Advantages of electronic approval systems

Electronic approval systems can provide a number of benefits apart from reducing demands on personnel. The system can be accessed 24 hours a day and can be used to provide consistent advice regarding approved indications for drug use. The institution may nominate certain standard indications and durations for which approval may be obtained via the computer, and then require individual approval for more complex indications or prolonged durations of drug use. This process focuses the expert prescriber's attention on the complex cases and does not burden them with 'routine' indications. However, the prescriber is still encouraged to think carefully about their own prescribing behaviour, which ensures that they are aware of hospital policy at the time of prescribing.

Electronic approval systems can provide access to guidelines at the time of prescription and thus address educative strategies for stewardship. They can generate electronic alerts or reminders, prompting review after a set period for complex patients being managed by the expert prescriber, and communicate advice explicitly to other clinical staff (doctors from other units, pharmacists, etc). Importantly, electronic approvals allow for easy data extraction and auditing of antimicrobial use, thereby facilitating feedback to individual prescribers, units and hospital committees.

Electronic approval systems do not function in isolation. They streamline the approvals process for general prescribers, pharmacists and nominated expert prescribers, and act as tools for AMS committees. They do not replace expert prescribers, but they can direct the attention of expert prescribers towards the most important patients.

2.5.5   Implementing electronic approval systems

The implementation of an electronic approval system requires careful planning. Important attributes of the system include high usability and meeting the needs of users within their context. In addition, the organisational structure surrounding the implementation of an electronic approval system needs to be assessed. Recently, Luu et al. assessed the readiness of hospitals in Victoria and Tasmania to adopt an electronic antimicrobial approval system.[68] They explored the human, organisational and technical aspects of 'readiness to change' and identified a number of domains in which hospitals could be assessed to identify 'gaps' that might need addressing. These included:

- technical readiness — integration requirements and access to information technology infrastructure

- resources — financial and human resources (e.g. provision of a project officer, antimicrobial pharmacist or ID specialist with dedicated time for stewardship activities)

- skills — training needs and prior experience of the project team and end users

- process readiness — project planning, system implementation, communication with staff, working rules, evaluation planning, feedback methods, and the ability to incorporate existing AMS strategies into the electronic workflow

- administrative readiness — executive support and high-level clinical champions.

Early observations from seven Victorian hospitals assessed in this way were that the hospitals differed significantly with regard to their readiness to adopt an electronic AMS system. Some hospitals had dedicated resources, but others lacked any additional staff time. Administrative support was generally high and most staff had the necessary skills to oversee implementation, but process readiness needed attention. Technical readiness was not identified as a barrier to readiness in any of the hospitals studied.[68]

Cultural factors are also important for successful implementation of electronic approval systems.[68] In a hospital where ID physicians or microbiologists have not previously played a prominent consultative role, staff will face additional barriers compared with hospitals with existing telephone or paper-based approval systems. These barriers need to be identified during the planning phase of the project and managed during implementation.

2.6 Antibiotic cycling

Antibiotic cycling is a restrictive strategy that involves withdrawing some classes of drug from routine use for a period of time and replacing them with another class of drug for empirical therapy, then reintroducing the original class later. This cycling aims to limit the emergence of resistance to the reserved antimicrobial. Antimicrobial cycling has primarily been studied in the intensive care unit setting.

Early pre and postintervention studies showed encouraging results when antimicrobials were cycled, with a fall in ventilator-associated pneumonia (VAP) due to resistant gram-negative bacteria and a higher likelihood of appropriate initial empirical drug choice. However, the 'before and after intervention' methodology of these studies meant that none of them had concurrent control groups, so other practices (e.g. infection control) may have also been modified during the studies.

More recent studies have cast doubt on the antibiotic cycling strategy, as they have shown the selection of drug resistance during the periods of cycling of each antibiotic class. For example, in a study by Van Loon et al.,[69] cefpirome, piperacillin-tazobactam or levofloxacin were each cycled for 4-month periods. Pathogens resistant to a particular cycling antibiotic were shown to be selected during each of the cycling periods. Similarly, Warren et al.[70] cycled four classes of antibiotic in 4-month blocks over two years and the proportion of bacteria resistant to the cycling class increased during the cycling periods.

Mathematical modelling studies now support heterogeneous antibiotic use rather than structured antibiotic cycling. Mathematical modelling by Bergstrom et al.[71] suggested that cycling would probably not be effective — homogeneous drug use for blocks of time was shown to be more likely to select for resistant isolates. The authors concluded that it is preferable to have mixed prescribing within a unit. The opinion of most experts in this field is that the evidence does not support antibiotic cycling as an effective strategy to control antibiotic resistance.

3 Antimicrobial review and prescriber feedback

Author: David Maxwell

3.1 Key points

- Practice review (audit) and feedback is a proven and effective strategy to influence prescribing behaviour.

- The review of antimicrobial prescribing practice and the provision of feedback to clinicians is an essential strategy for an antimicrobial stewardship program.

- The review of antimicrobial prescribing can be prospective or retrospective.

- Prospective review can involve strategies such as pre-authorisation and antimicrobial restrictions, with feedback being provided to the prescriber before the antimicrobial is administered.

- Retrospective review occurs after antimicrobial therapy has been initiated, and facilitates the provision of feedback based on results that may not have been available at the time of initiation.

- Although evidence suggests that antimicrobial prescribing review undertaken by a single health professional can be effective, a multidisciplinary team (e.g. including an infectious disease clinician, clinical pharmacist and microbiologist) is more likely to have a positive effect.

- Feedback should be tailored to the target audience and can be provided on a case-by-case basis or at a ward unit level.

- Provision of feedback should be structured to assist with the transfer of information.

3.2 Recommendations

! 3.2.1 Antimicrobial review and prescriber feedback is a routine part of clinical care.

3.2.2 The antimicrobial stewardship team is responsible for the provision of review and feedback at patient and unit level in wards with high antimicrobial usage (e.g. intensive care, oncology and haematology units).

3.3 Practice review

Practice review and feedback can be an effective method to influence prescribing behaviour that results in small to moderate changes in practice. This strategy has been used across a wide range of therapeutic areas in the healthcare setting. With respect to optimising drug use, the process of review commonly involves comparing current prescribing practice to an accepted standard or best practice, and feeding back variations in practice to the target audience. In the context of improving use of antimicrobials in the hospital setting, practice review often includes the use of a set of antimicrobial guidelines or an antimicrobial formulary as the standard to compare prescribing practice. Practice review and feedback has been incorporated into various strategies to influence prescribing behaviour, including the review of individual episodes of care and as part of broader quality improvement programs. In quality improvement programs, the process of practice review is often referred to as 'audit'.

In efforts to promote the prudent use of antimicrobials, a number of international peak bodies and organisations have included practice review/audit and feedback as a key strategy (or standard of practice) in the healthcare setting. The Infectious Diseases Society of America[1] has identified practice review as one of two core strategies — the second being formulary restriction and preauthorisation — that provide the foundation for an antimicrobial stewardship (AMS) program. The Healthcare Commission[72] (now the Care Quality Commission) in the United Kingdom recommended that '… the checking and provision of advice on antimicrobial prescribing is routinely undertaken' to ensure appropriate and effective use of medicines. Similar recommendations have been made in other countries, including Australia.[73]

3.4 Reviewing practice

This section outlines methods for reviewing prescribing practice: individual episodes of care and quality improvement programs.

3.4.1 Individual episodes of care

Review of antimicrobial prescribing may occur prospectively, before dispensing (front-end approach) or retrospectively, after therapy has been initiated (back-end approach). The front-end approach involves strategies such as pre-authorisation and antimicrobial restrictions, with direct feedback provided to the clinician before the drug is dispensed. Possible problems associated with this approach include a perceived loss of autonomy by prescribers and the need for 24-hour staffing, seven days a week. However, the front-end approach does provide an opportunity for additional education, as well as the provision of feedback regarding the particular episode of care. This approach, although more restrictive than the back-end approach, may be more effective in the overall appropriateness of antimicrobial prescribing.[34]

The back-end approach, or retrospective review of prescribing behaviour, 'permits empirical use of broad-spectrum antimicrobials, followed by postprescription review and then streamlining or discontinuing therapy'.[29] A number of benefits of postprescription review have been identified in the literature. These include:

- that recommendations will be informed by additional information not available at the time that the antimicrobials are prescribed, including results of radiologic and microbiologic tests[74]

- preservation of the autonomy of prescribers[12, 24]

- the opportunity for additional education when providing feedback[12, 24]

- the likelihood that this approach is less resource-intensive than the front-end approach.

Studies have reported that the retrospective review of antimicrobial therapy can occur 24–72 hours postprescription. A small nonteaching hospital reported significant improvements after the implementation of a postprescription review service provided on specific days of the week (three per week), rather than at a specific time interval after an antimicrobial had been prescribed.[41]

3.4.2 Quality improvement programs

The process of audit and feedback form part of established evidence-based quality improvement methodologies (e.g. Plan-Do-Study-Act [PDSA] or Drug Usage Evaluation [DUE] cycles) for the purpose of gathering data to be used as part of educational activities to influence prescribing behaviour (see Chapter 6 for more information on the education of prescribers). Typically, prescribing practice from multiple episodes of care (e.g. patients identified over a given time period) is evaluated against an accepted standard. Concordance with the standard is provided

as feedback to hospital staff as part of intervention and education. The process of audit and feedback is often repeated so that changes in prescribing practice can be monitored over time. Many quality improvement initiatives aimed to improve antimicrobial use have taken place within institutions and across multiple sites (e.g. Community Acquired Pneumonia: Towards Improving Outcomes Nationally [CAPTION] — see Appendix 1 for further details).

Further information on monitoring usage and quality improvement programs is provided in Chapter 5.

Prospective audit of antimicrobial use with direct interaction and feedback to prescriber, performed either by an infectious diseases physician or clinical pharmacist with infectious diseases training, can result in reduced inappropriate use of antimicrobials.[1]

3.5 Who should undertake the review and feedback process?

Models of the process of review and feedback in the literature include review by single health professionals (e.g. an infectious diseases [ID] physician or a clinical pharmacist) or by a multidisciplinary team (two or more members) representing specialties such as infectious diseases, pharmacy and microbiology. Both the individual approach and the team approach have been found to improve antimicrobial use. International peak bodies recommend that a multidisciplinary team or expert group be involved.[1,72] It is widely acknowledged that a multidisciplinary team working together to change practice is more likely to have a positive effect.[75]

Hospital pharmacists are well placed to identify antimicrobial use that requires review and can refer cases to the nominated AMS health professional or team. In addition, routine rounds by an AMS team in clinical areas (e.g. intensive care) can facilitate the process of practice review and feedback. For further information regarding the roles of the microbiology and ID services see Chapters 7 and 8, respectively.

3.6 What should the feedback include and how should it be provided?

This section outlines the kinds of feedback that should be included to facilitate improvements in prescribing practice for individual episodes of care and quality improvement programs.

3.6.1 Individual episodes of care

The 'appropriateness' of prescribing is an important concept in interventions for the improvement of prescribing practice, and papers have been published addressing this concept. One or more of the following might be used in an assessment of appropriateness:

- the decision to prescribe an antimicrobial

- the prescribing of an antimicrobial in accordance with local policy

- dosage
- duration of therapy.

Feedback, when required, should be directed to the prescriber immediately after a review of an individual episode of prescribing has been completed. Ideally, the provision of feedback to clinicians should be structured to assist in the transfer of information (e.g. ISBAR:[a] Introduction, Situation, Background, Assessment and Recommendation). This approach should be applied to both verbal and written methods of providing feedback.

Different methods of feedback after postprescription review were compared by Cosgrove et al.[74] The study looked at feedback provided by either a direct telephone call, a note in the medical record or a text message sent to the clinician's pager. The text messages and notes left in the medical record included detailed information on the recommended change, including the dose of the new agent and a rationale for the change. Recommendations were taken up by the attending clinician:

- 57.1% of the time with telephone call feedback
- 67.5% of the time with feedback via the paging system
- 73.7% of the time with feedback via a note in the medical record.

However, there was no statistical difference between the groups and the authors commented that this suggests that clinicians may be willing to implement changes regardless of how feedback is provided. They also suggested that hospitals with limited resources may be able to coordinate postprescription review and feedback of antimicrobial therapy effectively by conveying results by text or notes in the medical record. These methods are less resource-intensive than calling the clinician directly and they provide a clearer record than a telephone conversation, which relies on the clinician to write down the advice. However, direct telephone contact with the clinician allows further discussion and queries about the advice.

Interestingly, Cosgrove et al. found overall that medical teams were more likely than surgical teams to accept recommendations (68.1% versus 60.5%, P = 0.004). The authors noted that the surgical unit interns were more likely to seek consultant advice before making changes, compared with medical interns who were more likely to act independently. The surgical unit with the highest uptake of recommendations was staffed primarily by nurse practitioners who were able to modify patients' treatment regimens.

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a   ISBAR is a communication technique trialled in the Australian Commission on Safety and Quality in Health Care Clinical Handover Initiative Pilot Program. www.safetyandquality.gov.au/internet/safety/publishing.nsf/Content/PriorityProgram-05_ISBAR

3.6.2 Quality improvement programs

Quality improvement programs typically incorporate an agreed set of measures describing the quality of current practice. These are provided as feedback to hospital staff. Adherence of prescribing practice to accepted standards or guidelines is a common measure used in quality improvement initiatives aimed at influencing prescribing behaviour. Other measures include length of stay, readmission rates, clinical outcomes, mortality rates and drug use costs or consumption data.

As quality improvement programs involve the audit of multiple episodes of care, the data can be used to identify 'gaps' in practice at the level of a team or ward (compared with the review of individual episodes of care that focus on the practice of an individual). Feedback sessions can be tailored for the target audience and include the results of the audit and discussion around relevant guidelines and evidence, to educate hospital staff on best or accepted practice.

CAPTION, a multicentre quality improvement initiative supported by the National Prescribing Service, aimed to improve antimicrobial use in the management of community acquired pneumonia in Australian emergency departments.[76] As part of the initiative, two key measures were provided as feedback to hospital staff:

- documented use of a disease severity assessment tool
- concordance of antimicrobial prescribing with accepted national guidelines.

A set of tailored interventions were rolled out in participating hospitals, including one-on-one education visits, group education sessions that included the feedback of audit results and point-of-prescribing prompts. An overall 1.5-fold improvement in concordant antimicrobial prescribing was reported.

Cooke and Holmes propose the use of multifaceted interventions (care bundles) to improve appropriate antimicrobial prescribing in acute care and surgical prophylaxis.[39] They describe care bundles as a group of key evidence-based or logical actions, instituted over a specified timeframe, which if delivered together have a greater clinical effect than if each element was instituted individually. They suggest that hospitals using the care bundle approach to antimicrobial prescribing could improve local prescribing of antimicrobials and have ready access to performance measures of processes of care to serve as indicators for quality improvement programs. Further information on the use of care bundles to improve AMS prescribing is provided in Chapter 1.

Feedback may also be provided via weekly reports to prescribers, including aggregated data on compliance with guidelines and uptake of recommendations by clinicians.[78] Other forms of feedback include department-specific reports regarding compliance with local guidelines and newsletters highlighting therapeutic matters related to specific issues identified in the audit process.[78]

3.7 Published benefits

A Cochrane review published in 2005 reported on interventions to improve antimicrobial prescribing practices for hospital inpatients.[34] Interventions were classified as either persuasive — including audit and feedback — or restrictive (e.g. formularies, prior approval). The review looked at 10 published studies that used interrupted time series analysis to investigate the impact of persuasive interventions aimed to decrease inappropriate antimicrobial use. Five of the studies included the review and feedback of clinician prescribing. Four out of five of these demonstrated a significant improvement in measures of drug use data (grams or cost).

The Cochrane review identified only one paper that reported on the impact of persuasive interventions on microbiological outcomes. An antimicrobial program, including immediate practice review and feedback to clinicians, was initiated in a university teaching hospital in the United States after a sharp increase in the use of broad-spectrum cephalosporins and aztreonam was reported.[42] Data were collected for seven years after the implementation of the program. The authors reported a 22% reduction in the use of specific broad-spectrum antimicrobials and a significant decrease in nosocomial infections caused by *Clostridium difficile* and resistant Enterobacteriaceae (see Figure 3.1).

A randomised controlled trial that was not included in the Cochrane review investigated the effect of audit and feedback by an ID fellow and a clinical pharmacist on a group of prescribers, compared with a control group that received no feedback.[79] The review occurred 72 hours after the antimicrobial was prescribed. The impact of the intervention was assessed through cost savings, and clinical and microbiological outcomes. There was a significant cost saving of approximately US$400 per patient in the intervention group compared with the control group. There was no difference between the two groups in clinical or microbiological response.

A more recent study investigated the effect of prescriber feedback on antimicrobial prescribing behaviour and *C. difficile* infection (CDI) rates.[80] A narrow-spectrum antimicrobial policy was introduced across three aged care wards, with the aim of improving antimicrobial prescribing and reducing CDI. Feedback was provided to prescribers every 8–12 weeks, reporting antimicrobial usage (the number of notional 7-day courses per 100 admissions per month) and CDI rates. A copy of the policy was also provided to prescribers in the form of a laminated pocket-sized card.

Using interrupted time series methodology, Fowler et al. demonstrated a significant reduction in the use of broad-spectrum antimicrobials and an increased use of narrow-spectrum agents. CDI rates also fell, with incidence rate ratios of 0.35 (0.17–0.73, P = 0.009). It is interesting to note that the measure of antimicrobial use was used as part of the feedback to prescribers. The authors note that antimicrobial use was selected as a measure, rather than as defined daily doses per 1000 bed-days, to help doctors visualise the percentage of patients treated with individual antimicrobials.
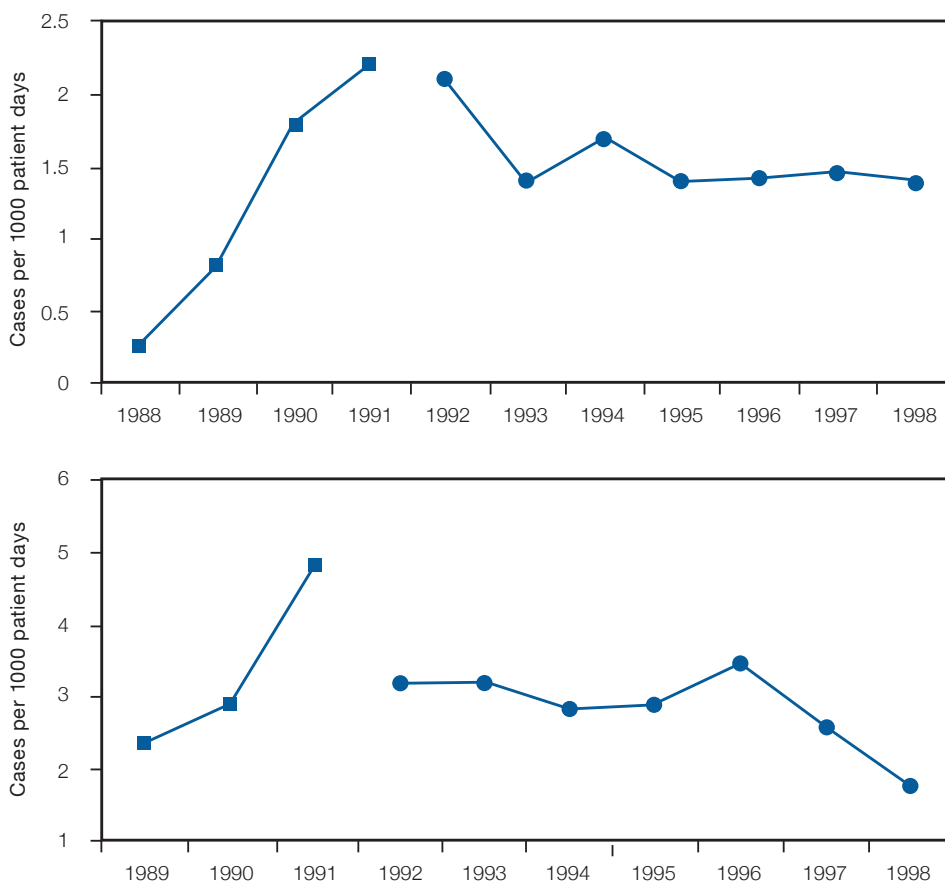
Source: Carling et al. (2003)[42]

Figure 3.1   **Rates of nosocomial *Clostridium difficile* and resistant Enterobacteriaceae infections, expressed per 1000 patient days, before (1989–91) and after (1992–98) implementation of the antimicrobial management program; top, *C. difficile*; bottom, resistant Enterobacteriaceae**

The options of de-escalation, streamlining, switching from intravenous to oral delivery or ceasing antimicrobial therapy may not demonstrate an improvement in immediate patient outcomes compared with continuation of broad-spectrum therapy. Demonstrating no additional harm or adverse events when optimising antimicrobial therapy is therefore an important consideration, in addition to any cost savings that may be realised. Where available, data demonstrating patient safety outcomes should be included as part of the feedback or education process when rationalising antimicrobial therapy.

4 Point-of-care interventions

Author: John Turnidge

4.1 Key points

- Point-of-care interventions are a valuable component of antimicrobial stewardship.

- Point-of-care interventions provide direct feedback to the prescriber at the time of prescription or laboratory diagnosis, and provide an opportunity to educate clinical staff on appropriate prescribing.

- Examples of point-of-care interventions include:

  » reviewing appropriateness of choice of antimicrobial

  » directed therapy based on microscopy and other rapid tests

  » directed therapy based on culture and susceptibility test results

  » dose optimisation

  » parenteral-to-oral conversion

  » therapeutic drug monitoring

  » automatic stop orders.

- What interventions are selected, how they are delivered and by whom, will be determined by local resources and the expertise available.

4.2 Recommendations

4.2.1 Point-of-care interventions are included in all antimicrobial stewardship programs.

4.3 Benefits of point-of-care interventions

Point-of-care interventions (POCIs) are interventions that occur at the ward level with the treating medical team, often soon after empirical therapy has been initiated. They are one of the most effective aspects of antimicrobial stewardship (AMS) in hospitals. Although POCIs are supplemental stewardship activities according to the Infectious Diseases Society of America/Society for Healthcare Epidemiology of America,[1] they form an important component of feedback following prescribing review. They can improve patient management and patient outcomes, and provide excellent opportunities to educate clinical staff on rational prescribing. POCIs can be delivered by a stewardship pharmacist, a stewardship team or during an infectious diseases (ID) consultation.

POCIs are a part of many successful stewardship programs.[42, 81] They are generally implemented simultaneously with other measures, which makes it difficult to show the benefits of these interventions alone. However, POCIs are widely recommended, especially parenteral-to-oral conversion, daily review with de-escalation, and dosage optimisation,[3, 15, 18] and are included in best practice guidelines for AMS.[1, 16-18]

Despite their effectiveness, a major barrier to effective POCIs can be a physician's reluctance to de-escalate from broad-spectrum empirical therapy if the patient is improving. The attitude can be 'when you're on a good thing, stick to it'. This barrier is less common among younger prescribers who have had more exposure to the concepts of evidence-based medicine.

4.4 Directed therapy based on the prescription of a restricted antimicrobial

POCIs are used to effect hospital policies on antimicrobial prescribing (e.g. formulary restrictions). They are most effective when they take place within minutes or hours of a prescription or laboratory result being generated. A common approach is to activate a POCI whenever a prescription is received by the pharmacy for an antimicrobial that does not conform to drug and therapeutics committee prescribing (restriction) policy. For example, an inpatient prescription written by a non-authorised prescriber for a restricted antimicrobial (e.g. as a third-generation cephalosporin) is received by the pharmacy. The pharmacist may contact the prescriber directly and request that they seek authorisation, or they may refer the matter immediately to an ID physician, clinical microbiologist or registrar.

Either method permits the exchange of clinical and laboratory information so that a judgement can be made about the appropriateness of the antimicrobial. Such judgements should be based on:

- agreed treatment standards and protocols
- the individual patient's clinical circumstances.

This method of real-time communication leads to the formal endorsement of the prescription or a discussion about appropriate alternative treatments. Commonly, the recommended alternative will be a narrower spectrum agent with known equal efficacy, although there will be occasions when the appropriate alternative is another equally or even more restricted agent.

Seto et al.[82] tried a more formal approach to delivering POCIs. They used a method of immediate concurrent feedback to communicate with the prescriber such that each prescription for a restricted agent led to a same-day review by a small designated authoritative group. The group then communicated their decision to the prescriber. However, this process may be less immediate than the one described above.

4.5 Directed therapy based on microscopy results and other rapid tests

For a small number of conditions, the choice of empirical therapy can be improved using microbiology results that are available minutes or hours after specimen collection. The best example is meningitis — common clinical practice is to make a semi-definitive diagnosis based on the collection of cerebrospinal fluid (CSF) via lumbar puncture, and fast specimen processing that might include the use of on-call staff after hours to conduct cell counts, Gram stains and antigen tests. With appropriate caveats around the safety of collecting CSF, this should be considered standard practice for suspected meningitis. Similarly, the choice of empirical therapy can be directed in:

- vaginitis — microscopy readily distinguishes between candidiasis, trichomoniasis and bacterial vaginosis, so the choice of treatment should await the results

- urethritis/cervicitis — microscopy can readily diagnose gonococcal disease, and is widely used in sexually transmitted disease clinics to decide on empirical therapy

- urinary tract infection (UTI) — dipstick testing for leukocyte esterase, protein and blood; when all three are negative, there is a very high negative predictive value for UTI, which warrants the withholding of empirical antibiotics for UTI

- protozoal gastroenteritis — definitive diagnosis for giardiasis, amoebiasis and some other less common protozoan parasites is possible on microscopy alone.

In many clinical settings, including hospitals, microscopy is underused. There is no published literature investigating the benefits (or otherwise) of awaiting microscopy results before deciding on appropriate antimicrobial use.

4.6 Directed therapy based on culture and susceptibility test results (de-escalation or streamlining)

Recent studies reporting increased mortality with inappropriate or delayed empirical antimicrobial therapy have led to advocacy of early broad-spectrum antimicrobial therapy for a number of hospital infections. Although this approach

reduces the risk of inadequate therapy, it may increase the risk of selection or acquisition of strains resistant to these agents, which may subsequently be very difficult to treat.[12]

Bacterial culture results, including identification and susceptibility test results, are usually available between 48 and 72 hours after specimen collection. Results of these tests should be used to improve antimicrobial choices and optimise therapy through streamlining or de-escalation therapy.[1, 12, 16] This approach uses the principle that empirical prescribing should be broad enough to cover the likely pathogens and their associated resistances, but should be converted to definitive or targeted treatment when the pathogen and its susceptibilities are known ('start broad, finish narrow').

Antibiotic therapy should be streamlined at the earliest opportunity, where possible using the results of laboratory tests.[16]

There is good evidence that encouraging the treating team to modify therapy (if necessary) reduces antimicrobial exposure and makes cost savings. Typical POCIs in this category are:

- changing the antimicrobial agent

- ceasing additional antimicrobials not known to add benefit to outcomes

- ceasing antimicrobial therapy altogether (with negative culture results).

4.7 Dosing schedule optimisation

Optimising antimicrobial dosing is an important part of AMS and there is good evidence to support the effectiveness of this intervention.[1]

Pharmacists can play an important role in identifying deviations from recommended dosing schedules when reviewing medication orders and dispensing prescriptions. This provides an opportunity to discuss the doses and dosing frequency immediately with the prescriber, with a view to optimising a patient's dosing schedule. The pharmacokinetic and pharmacodynamic features of the antimicrobial should be taken into account in this discussion.

Antimicrobial dosing schedules can be optimised in a range of ways:

- checking doses against a prescribing standard such as *Therapeutic Guidelines: Antibiotic*[19] and adjusting them when they are not comparable (e.g. excessive doses of beta-lactams are commonly prescribed)

- adjusting dosing interval where circumstances are appropriate, for example

  » changing aminoglycoside from three times daily to once daily for almost all indications

  » considering a switch to continuous infusion of short half-life beta-lactams (e.g. piperacillin/tazobactam, cefepime, meropenem) for some infections,[15, 23] especially those requiring treatment beyond 5–7 days

- monitoring antimicrobial levels in an individual patient and adjusting dosing to maximise efficacy, while minimising toxicity (e.g. with aminoglycosides and azole antifungals); the *Therapeutic Guidelines: Antibiotic*[19] provides guidance on the monitoring of aminoglycosides and vancomycin.

Anecdotally, convincing prescribers to change dosing regimens can sometimes be challenging, especially if it involves reducing the initially prescribed doses.

4.8   Duration

The weight of evidence suggests that resistance selection increases with longer courses of antimicrobials.[83-84]

Incorrect duration of antimicrobial use is a frequent problem in hospital prescribing. Surgical prophylaxis that is administered beyond one dose or one day is a common example. Hospitals should have policies for the prophylactic use of antimicrobials that state that a single dose is the preferred option.[18] (See example in Appendix 2, Section A2.1.)

Microbiologists and ID physicians are frequently asked for advice on duration of treatment. Almost all infections have standard treatment durations. Duration of therapy often needs to be tailored to individual responses to treatment, especially considering delayed responses in immune compromised patients. Nevertheless, in the context of advising on therapy, antimicrobials should generally be prescribed for a maximum of seven days, or a shorter period if this is clinically appropriate.

It is important to embed a prescribing culture that includes daily review and setting a maximum duration of treatment, unless there is a clear indication in the medical record that therapy should be continued.[18]

4.9   Parenteral-to-oral conversion

The acquisition and administration costs of intravenous therapy are almost always higher than those of oral therapy. However, oral therapy is preferred for other reasons. It is in the best interests of the patient to be discharged to their home environment once they are clinically stable and able to take oral therapy. Continued hospitalisation is associated with the risk of a new multidrug-resistant infection, increase in *Clostridium difficile* infection, or a preventable adverse event such as an infection from the intravenous line. Encouraging a switch to oral therapy once the patient has shown significant clinical response to treatment is a well-studied strategy that has proven value.[1, 3, 85]

Certain antimicrobials have near complete bioavailability and some oral therapies have been shown to be as effective as parenteral therapy.[15] For agents available in both oral and parenteral formulations — and with high bioavailability — a switch to oral treatment as soon as it is clinically safe to do so is relatively simple. Examples include fluoroquinolones, linezolid, fluconazole and voriconazole.[15] For some parenteral agents, there is no obvious oral equivalent (e.g. vancomycin), so alternative oral agents of known efficacy are used. Although expensive, the use of

linezolid in the treatment of methicillin-resistant *Staphylococcus aureus* (MRSA) infection is associated with a shorter length of hospital stay compared with parenteral vancomycin, which can potentially free up hospital beds.[15]

Prescribers are often reluctant to convert to oral treatment in patients who are still febrile, but studies have shown that if there are other clinical objective criteria showing that the patient has responded well, the fear of conversion is unfounded.[1] Defined criteria can be established and agreed upon that allow a stewardship team to expedite the change to oral therapy. The *Therapeutic Guidelines: Antibiotic*[19] provide guidance on when oral therapy should be used in preference to parenteral therapy. (See Section A2.1 in Appendix 2 for examples of local guidelines and educational materials.)

A systematic plan for parenteral to oral conversion of antimicrobials with excellent bioavailability, when the patient's condition allows, can decrease the length of hospital stay and health care costs.[1]

The National Health Service summary of best practice on antimicrobial prescribing[18] recommends as a general rule that intravenous antimicrobials should only be prescribed for two days, after which the prescription should be reviewed and, if appropriate, the patient switched to oral therapy.

Benefits of the oral switch include:[1]

•   lower treatment costs

•   reduced morbidity from (now removed) intravenous lines

•   reduced length of stay

•   higher patient satisfaction.[86]

4.10 Who should provide point-of-care interventions?

In general, POCIs involve one or two relevant individuals providing information and recommendations to the prescriber. The individuals may or may not be formal members of an AMS team, but could be any trained member of pharmacy, ID or clinical microbiology services. The role of these services in providing POCIs is further discussed in Chapters 7–9. Institutions necessarily vary how they deliver interventions (including by whom); this will be determined by local resources and the availability of expertise.

5 Measuring the performance of antimicrobial stewardship programs

Authors: David Looke and Margaret Duguid

5.1 Key points

- Monitoring and analysis of antimicrobial usage is critical to understanding antimicrobial resistance and measuring the effects of stewardship interventions.

- Continuous surveillance of the appropriateness of antimicrobial prescribing should be the ultimate aim of any stewardship program.

- Reporting and analysis of ward and hospital antimicrobial usage data is useful in monitoring trends and identifying areas for evaluating appropriateness of prescribing.

- Process and outcome measures are an integral part of any quality improvement program and should be incorporated into the hospital's antimicrobial stewardship plan.

- Process indicators can be used to target and evaluate initiatives to improve prescribing. Providing timely feedback in a format that can be interpreted and used by clinicians is important.

- The introduction of an individual patient electronic medical record linked with electronic prescribing and medication management systems will improve surveillance of antimicrobial usage and appropriateness of prescribing, and enable more efficient targeting of interventions.

5.2   Recommendations

!   5.2.1   Antimicrobial usage data is collected and regularly reviewed to identify areas for improvement.

5.2.2   Quality indicators are monitored to assess appropriate prescribing practice and compliance with policy.

5.2.3   Information technology resources are available for:

» monitoring antimicrobial usage

» auditing process indicators

» measuring outcomes of the antimicrobial stewardship program.

5.2.4   Antimicrobial usage data is interpreted together with infection control and antimicrobial resistance data.

5.3   Assessing antimicrobial stewardship activities

Successful antimicrobial stewardship (AMS) programs include all the elements of successful quality improvement programs and measuring the effectiveness of program activities is a key component. In AMS programs, this usually includes measuring antimicrobial use, auditing the quality of prescribing, and monitoring process and outcome indicators. The information can then be used to provide feedback to prescribers, and inform the AMS team and drug and therapeutics committee of the effect of stewardship initiatives on antimicrobial use and resistance patterns. This chapter focuses on aspects of the effective use of surveillance data in stewardship programs, and reviews the use of process and outcome indicators to assist with targeting initiatives to improve prescribing. A detailed discussion on using quality improvement strategies to implement effective AMS is presented in Chapter 1.

Hospital administrative support for the infrastructure (including information systems) required to measure and monitor antimicrobial use and the outcomes of AMS interventions is considered essential to the success of an AMS program.[1]

5.4 Effective use of surveillance data in stewardship programs

Effectiveness of prescribing can be measured by the quantity of agents prescribed and by the quality of the prescribing (i.e. appropriateness for a given indication). Continuous prospective monitoring of the appropriateness of antimicrobial prescribing should be the ultimate aim of any stewardship program. However, this requires real-time knowledge of:

- the provisional and confirmed diagnosis of every patient
- patients' underlying co-morbidities
- the agent (or agents) prescribed, including details such as dose, duration and route
- the outcome of treatment.

Ideally, these data would be collected electronically; however, this is not possible with the information systems now available in Australia. Currently, this form of prospective surveillance is only possible using highly trained clinicians to review individual charts, which is a time-consuming and resource-intensive task. This type of review is often completed as a 'snapshot' survey or point prevalence study and is discussed in detail in Section 5.6.1.

A comprehensive review of current local and international surveillance systems for antimicrobial use was published by Duguid et al.[25] (see Appendix 1). The review addresses the reasons for monitoring antimicrobial use data, methods of surveillance (measurement, definitions and reporting), and existing Australian and international surveillance systems. Information from the review is not repeated in this chapter and it is recommended that Appendix 1 is read in conjunction with this chapter.

5.5 Measuring the volume of antimicrobial usage

To standardise the quantification of antimicrobial use and allow comparisons over time or between units and hospitals, it is recommended that drug use data are expressed as defined daily dose (DDD) per 1000 occupied bed-days.[1, 87-88] Because DDDs are based on adult dosing, these measurements are not suitable for determining antimicrobial use in paediatric units. Use is usually reported by antimicrobial type or class using the anatomical therapeutic chemical (ATC) classification.

Another measure used to monitor the volume of antimicrobial use is the prescribed daily dose. The prescribed daily dose is calculated by dividing the total grams of the antimicrobial agent used by the number of grams in a locally used average daily dose of the agent given to an adult patient. Prescribed daily dose is a measurement of the number of patient days that treatment has been given, whereas DDD is a measurement of total amount of antimicrobial used. Both measures can be derived from pharmacy data (see Section 5.5.1 below). Both are useful for monitoring usage. Refer to Appendix 1 for further information on surveillance methods.

5.5.1 Reporting and monitoring usage data at a local level

Information on antimicrobial use is generally available from hospital pharmacy information systems. Data on inpatient use is obtained from the volume of ward stock issued combined with individual patient issues. It may be reported monthly, quarterly or annually, preferably as DDDs. Ward stock use is not generally linked to individual prescribers, so the data are purely measures of the volume of medicines prescribed in a given time. These data can be reported as whole-of-hospital data or broken down into individual ward or division information. Specific antimicrobials or antimicrobial groups can be targeted or total antimicrobial consumption measured. Although expenditure data have severe limitations, since costs are affected by purchase contracts, formulary changes and variations in ordering patterns, they can be helpful to identify where dollars are being spent[15] and to track any savings from stewardship activities.

Measurement of antibiotic consumption should be performed with regular benchmarking of figures and discussion between prescribers, pharmacists and infection specialists.[16]

Since much of the consumption data cannot be linked to individual patients, and given that many agents are used for a narrow band of indications, large fluctuations can appear in small ward populations. An example of surveillance of antifungal agents at the ward level is shown in Figure 5.1, which illustrates monthly amphotericin B use in a large intensive care unit (ICU).
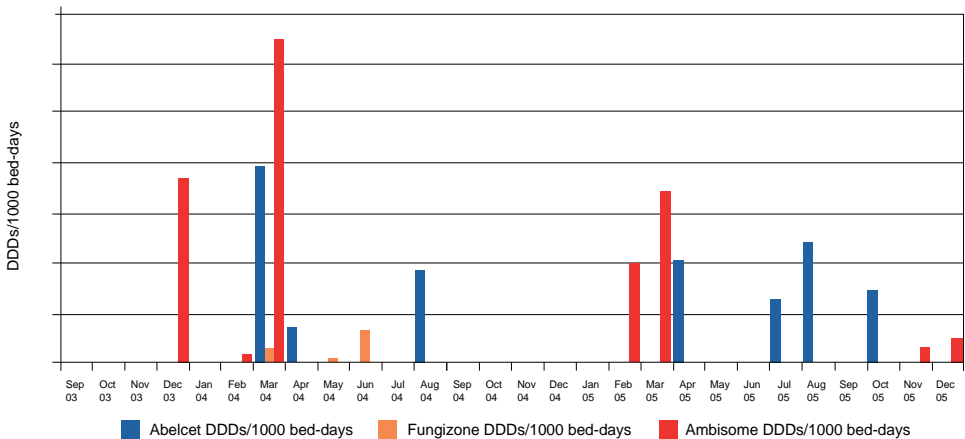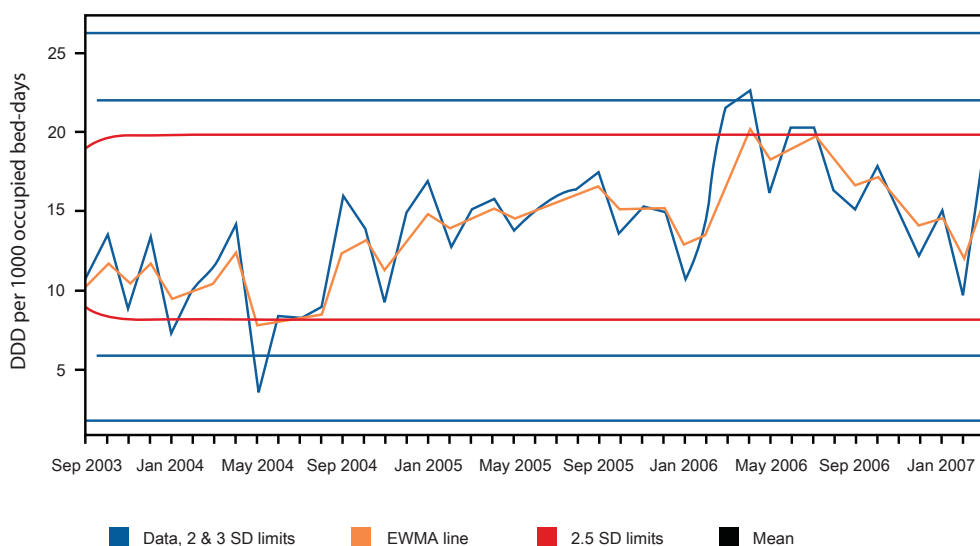

DDD = defined daily dose
Source: Dr David Looke 2010

Figure 5.1   Amphotericin B use in an intensive care unit

Another limitation to using ward-based data is that data have direct relevance to the individual prescribers only where a ward corresponds closely to a medical or surgical specialty unit (e.g. ICU, oncology/haematology).

5.5.2 Use of control charts to monitor trends in prescribing

Reviewing data on ward issues to determine changes in prescribing can be problematic. Clustering of infections and the use of antimicrobials in a time period subsequent to that when the drugs were issued by pharmacy can cause wide variations in the volumes used of many of the antimicrobial agents available in hospitals.[89] Continuous monitoring of ward use data using methods such as control charts can be useful for identifying trends in prescribing and may signal that inappropriate prescribing of specific drugs is occurring. This can act as a trigger for further investigation such as evaluation audits of the drugs used in a ward or unit. Control charts can also be used to identify real improvements over time. Time series charts such as a Shewhart chart account for random variation (see Figure 5.2). Such charts should ideally have control limits.[89]
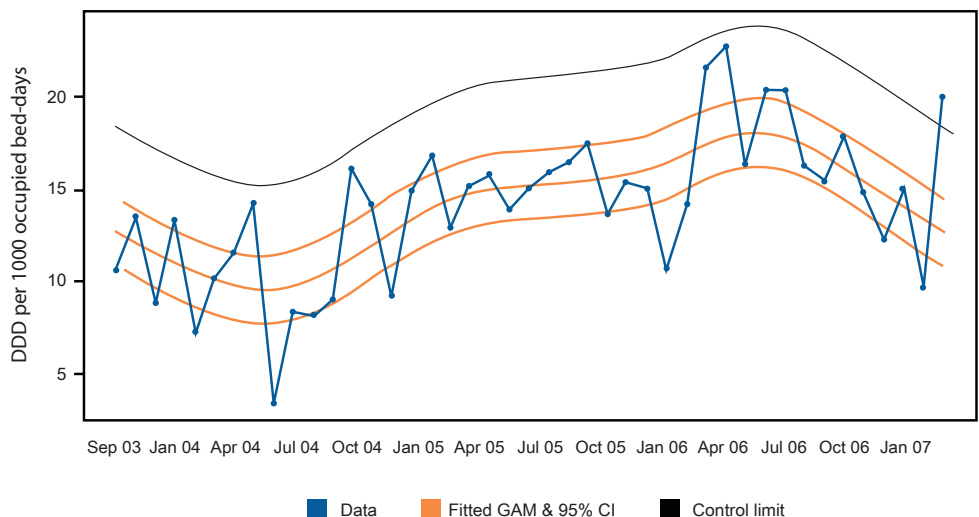

DDD = defined daily dose; EWMA = exponentially weighted moving average; SD = standard deviation

Figure 5.2   Third generation cephalosporin use in inpatients in an Australian teaching hospital (defined daily doses per 1000 bed-days) Shewhart/EWMA chart from September 2003 to March 2007

Morton et al.[89] have researched these types of data for some years and believe that the generalised additive model (GAM) chart is superior to the traditional Shewhart chart or the simple determination of a trend in a time series. Examples of the same data presented in three different formats are provided for comparison: the Shewhart chart (Figure 5.2), the GAM chart (Figure 5.3) and a simple bar chart, where the significance of the trends is not apparent (Figure 5.4). The data represents the inpatient use of third-generation cephalosporins in an Australian teaching hospital over a 42-month period. The Centre for Healthcare Related Infection Surveillance and Prevention (CHRISP) in Queensland reports antimicrobial use in all Queensland Health inpatient facilities using DDDs and Shewhart displays (see Section 5.7).

Conventional Shewhart control charts rely on predictable data values so that the average and its variability can be determined. This may be difficult to achieve with hospital antimicrobial data and a Shewhart chart may give misleading information. A modified control chart based on a GAM can take this variability into account and allow the display of more appropriate control limits.[89] (See Figure 5.3.)

Figure 5.3 displays monthly data values (blue), a smoothed predicted average value (inner orange line) and its confidence limits (outer orange lines), and an upper two standard deviation equivalent control limit (black line). The confidence limits describe the precision of the predicted average value and may be used to detect statistically significant trends. The control limit detects high monthly values that may be outliers.[89]

CI = confidence interval; DDD = defined daily dose; GAM = generalised additive mixed model

Figure 5.3   Third-generation cephalosporin use in inpatients in an Australian teaching hospital (defined daily doses per 1000 bed-days), GAM chart from September 2003 to March 2007
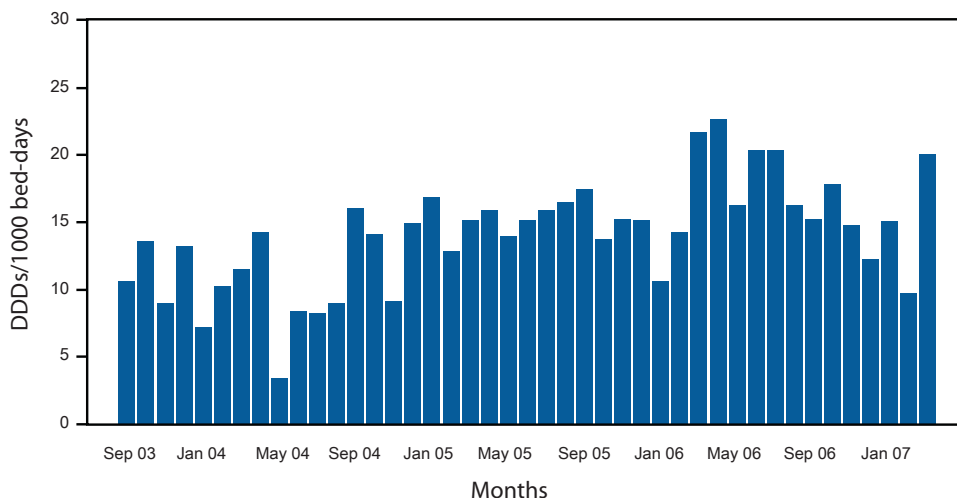
DDD = defined daily dose
Source: David Looke 2010

**Figure 5.4   Third-generation cephalosporin use in inpatients in an
Australian teaching hospital (defined daily doses per 1000
bed-days), September 2003 to March 2007**

There is only a small amount of literature on this form of surveillance and feedback
in terms of effectiveness on reducing rates of antimicrobial resistance. This area was
well reviewed by Madaras-Kelly in 2003,[90] who reported that the only study that
indicated that infection control surveillance data feedback could affect resistance
rates was in the National Nosocomial Infections Surveillance System — Project
Intensive Care Antimicrobial Resistance Epidemiology (NNIS-ICARE) program
report. Most studies have focused on single drug and single organism combinations.
Fowler et al.[80] describe a prospective controlled interrupted time series study
using feedback on antimicrobial usage and *Clostridium difficile* infection (CDI) rates
to reinforce antimicrobial policy and reduce CDI. The broader effects of changing
prescribing habits on resistance patterns have not been assessed.

Despite the limitations, broad-scale surveillance of antimicrobial use data obtained
from hospital pharmacy information systems can be useful on many levels. It
currently provides the most accurate indication of which antimicrobials are being
used and where it brings trends in prescribing into focus, and may allow more time-
efficient use of drug usage evaluation (DUE) resources to direct them towards real
changes in prescribing volumes. Until electronic prescribing — integrated with an
electronic medical record that has antimicrobial prescribing surveillance 'hardwired'
into its design — is implemented widely in the Australian hospital environment,
broad-scale use data from pharmacy information systems will remain the only
quantitative measure of total antimicrobial consumption available.

5.6 Measuring the quality of antimicrobial usage

Continuous prospective monitoring of the appropriateness of antimicrobial prescribing should be the ultimate aim of any stewardship program. Measurements of the quality of prescribing can provide assurance that the most effective therapy is being given, and the risk of poor outcomes, including antimicrobial-related adverse events, is being reduced.

In the absence of electronic systems to efficiently report data, the appropriateness of prescribing is usually measured by reviewing patient notes, using prevalence surveys such as 'snapshots' of elements of antimicrobial prescribing in a healthcare facility or clinical audit as part of a DUE program.[3–4, 50, 88, 91–92] Data from these surveys can be used by the AMS team and drug and therapeutics committee to monitor the effectiveness of an intervention and as part of educational activities to influence prescribing behaviour.

5.6.1 Prevalence surveys

Prevalence surveys are an effective tool to improve the quality of antimicrobial prescribing. They allow problem areas to be targeted and enable more intensive audits, leading to further interventions to improve prescribing. They are also useful for measuring the effects of interventions. Such surveys are most useful when repeated at regular intervals.

Point prevalence or 'snapshot' surveys

Point prevalence or 'snapshot' surveys have the advantage of being resource-efficient; however, they can only provide feedback on limited elements of prescribing in the facility and may not consistently reflect practice within a unit or hospital.[91] Point prevalence surveys are done at a single site on a single day. The data are often collected from one data source — the medication chart. The type of information provided by these surveys may include the percentage of patients prescribed antimicrobials, the range and volume of agents prescribed, percentage of 'restricted' antimicrobials prescribed, number of antimicrobials per patient, duration of therapy, dosing and dosage interval, and time for intravenous-to-oral switching.[3-4, 88] Prophylactic use can be assessed by reviewing surgical patients who were prescribed antimicrobials in the previous 24 hours.

Linking survey information with clinical data gathered from other sources (such as indication, prophylaxis or treatment, nature and severity of the infection and details of antimicrobial therapy received) can enable a better assessment of the appropriateness of prescribing, including prescribing in accordance with clinical guidelines.[88] However, this type of survey is more resource-intensive.

Serial point prevalence studies conducted at regular intervals are a practical method for studying hospital antimicrobial use in the absence of computerised prescribing. They provide hospitals with baseline information on current antimicrobial usage from which specific targets for intervention can be identified and evaluated

in subsequent audits. Dean et al. describe a series of three standardised point prevalence studies that used pharmacists to collect the data on all patients prescribed systemic antimicrobials admitted to four hospitals.[92] They found the data collection method reliable and suggest one or two point prevalence studies a year sufficient to provide ongoing monitoring of antimicrobial use.

Willemsen et al.[4] performed point prevalence surveys on all inpatients in a large teaching hospital in the Netherlands, assessing antimicrobial prescribing and analysing appropriateness judged against current institutional guidelines. They also identified patients who did not receive antimicrobial therapy even though it was indicated. Six consecutive one-day surveys were conducted at six-monthly intervals over a three-year period, using infection control practitioners to collect data from medical and nursing records. Data were used to identify and measure the effects of interventions to improve antimicrobial use.

Clinical pharmacists are ideal personnel to collect data, with a stewardship pharmacist coordinating data collection,[88] and infectious diseases physicians or clinical microbiologists involved with assessment of appropriateness.[91]

Point prevalence surveys can be used to measure and compare antimicrobial use in multiple sites — the data can be used to inform local and national audits and support prescribing initiatives.[91]

5.6.2 Audit and feedback

The use of audit and feedback in stewardship quality improvement programs, including DUE studies, is further discussed in Section 3.6.2. Auditing adherence to antimicrobial policies and guidelines are fundamental activities in any AMS program. Examples of the types of audits that may be considered include:

* reviews of drug charts, with antimicrobial prescriptions assessed according to predetermined criteria of appropriateness

* chart reviews of treatment of selected infectious diseases, identified by positive microbiological tests

* reviews of 'restricted drugs' to ensure that proper approval processes have been followed (the use of electronic approval systems described in Chapter 2 facilitates these exercises).

5.7 Reporting and use of data at state and national levels

In Australia, there is some state and territory-wide reporting on antimicrobial drug use, and more recently some national reporting through the National Antimicrobial Utilisation Surveillance Program (NAUSP), originating in South Australia.

South Australia and Queensland have state-based programs that collect and report on in-hospital antimicrobial use data. In South Australia, hospitals contributing data receive monthly reports detailing antimicrobial use density rates in the form of

time series graphs, including specific use rates for ICUs. Corresponding state-wide aggregate reports are supplied for comparison and are publicly available. CHRISP in Queensland has initiated standardised reporting of antibiotic use in all Queensland Health inpatient facilities using DDDs and Shewhart displays. The data are reviewed twice a year by the Queensland Health Medicines Advisory Committee and are used to direct antimicrobial use evaluation projects.

At a national level, NAUSP collects aggregate data from hospitals in all Australian states and territories. The program currently collects data from 29 major public and 2 private hospitals, representing approximately 60% of Australian tertiary referral beds. Separate usage rates are currently reported for ICUs. Contributing hospitals receive bimonthly reports of hospital inpatient antimicrobial usage, reported as ICU and non-ICU usage. Corresponding 'national' rates, calculated from aggregate data, are included for comparison. Further information on NAUSP is provided in Appendix 1, Section A1.6.2.

At a local level, data from these programs can be used to monitor the effect of AMS activities on drug use and to benchmark ICU and non-ICU use data against peer hospitals (see Case study 2 in Appendix 1). These systems and other national surveillance programs are reviewed extensively in Appendix 1.

Using larger scale reporting systems to draw comparisons across hospitals, areas, states and territories, or even countries has potential problems. Case-mix and regional variations in the incidence of particular infectious diseases or antimicrobial resistance can confound the results. Kuster et al.[93] attempted to correlate antimicrobial consumption with a case-mix index across a group of hospitals in Switzerland. They found that a significant correlation existed and suggested that case-mix distribution should be taken into account when analysing large sets of antimicrobial use data. Kritsotakis et al.[94] attempted stratification of surveillance data by ward type in an effort to reduce confounding by patient mix. Although this was useful to the individual facility in indicating trends, there were major problems with comparisons between facilities.

This type of surveillance is useful for monitoring fluctuations and trends over time — statistically significant increases or decreases in use can be investigated to determine whether or not they are evidence of inappropriate prescribing.

5.8   Process and outcome measures of stewardship activities

Process and outcome measures of antimicrobial policies should be audited.[16]

5.8.1   Process measures

Performance measurement is an integral part of the quality improvement cycle and a number of indicators for appropriate antimicrobial prescribing have been reported in the literature. These are predominately process indicators such as rates of adherence to guidelines, appropriateness and timeliness of therapy for a given infection, advice acceptance rates and rates of concordance with susceptibility

reporting.[17, 23, 35, 95] Measurement of these rates may occur as an intermittent audit — as part of the evaluation of a stewardship intervention — rather than as ongoing continuous surveillance. When instituted as regular cycled audits and reported as indicators (sometimes termed key performance indicators or KPIs) they can be useful instruments to maintain prescribing performance at an appropriate high level.

Feedback in a format that can be interpreted and used by clinicians is important. Indicator results may be presented dynamically in the form of run charts or control charts (with control limits) as this allows clinicians (and stewardship team members) to assess whether the process is stable and identify real improvements over time.[95]

A limitation of indicators is that organisations may focus their efforts on only one aspect of performance to the detriment of others, leading to the 'gaming' of results.[96] This applies particularly to publicly reported measures. Unexpected consequences include the skewing of treatment priorities and the promotion of unnecessary antimicrobial use.[97] Wachter et al. suggest that key end users need to be involved in the development of KPIs and the assessment of validity, reliability, impact and costs should occur within one to two years of implementing quality measurement and reporting programs.[97]

Nathwani et al.[87] reviewed the development of indicators for antimicrobial control programs and concluded that potential indicators should be prioritised to maximise cost-effectiveness and be multidisciplinary in their development to ensure ownership by relevant clinical groups. A quality indicator for glycopeptide prescribing was cited as an example. Cooke and Dean[77] described a similar indicator for glycopeptide prescribing and showed that a simple audit tool for vancomycin prescribing uncovered a substantial number of problems with the prescribing of glycopeptides.

The NSW Therapeutic Advisory Group has published a compendium of indicators[95] for the quality use of medicines in Australian hospitals. They include indicators relating to antimicrobial prescribing, such as the percentage of:

- patients undergoing specified surgical procedures that receive an appropriate prophylactic antibiotic regimen

- prescriptions for restricted antibiotics that are concordant with drug and therapeutics committee approved criteria

- patients with a toxic or subtherapeutic aminoglycoside concentration whose dosage has been adjusted or reviewed prior to the next aminoglycoside dose

- patients presenting with community acquired pneumonia that are prescribed guideline concordant antimicrobial therapy.

Other important indicators to measure are the time to first antimicrobial dose, such as in patients presenting to hospital with bacterial meningitis or severe sepsis.

5.8.2 Outcome indicators

In addition to using process measures, Dellit et al.[1] also recommend using outcome measures to determine the impact of AMS on antimicrobial use and resistance patterns (i.e. did the process implemented reduce or prevent resistance or other unintended consequences of antimicrobial use?).

Clinical outcome measures such as mortality, readmission rates and length of hospital stay may be too indirectly related to appropriate antimicrobial prescribing to be an accurate reflection of the performance of AMS programs. However, a reduction in bacterial resistance and a decrease in CDI infection are proposed as key metrics to consider when evaluating the effect of AMS.[37] Further evidence attesting the success of using such outcome measurements is awaited.

6 Education and competency of prescribers

Authors: Celia Cooper and Margaret Duguid

6.1 Key points

- Education in safe and judicious antimicrobial prescribing is an important element of any antimicrobial stewardship program.

- Education of all health professionals involved in antimicrobial prescribing should begin at undergraduate level and be consolidated with further training throughout the postgraduate years.

- Active education techniques, such as academic detailing, consensus-building sessions and educational workshops, have been shown to be more effective in changing prescribing behaviour than passive dissemination of information.

- Pharmaceutical industry-sponsored activities have been shown to negatively influence prescribing behaviour.

6.2 Recommendations

6.2.1 Prescribers are taught to prescribe according to the *Therapeutic Guidelines: Antibiotic*[19] in undergraduate, postgraduate and professional development programs.

6.2.2 Hospitals are responsible for educating clinical staff about their local antimicrobial stewardship programs.

6.2.3 Hospitals enact policies on the interaction between prescribers and the pharmaceutical industry, based on national guidance. Prescribers are educated about the influence of pharmaceutical industry activities on prescribing behaviour.

6.2.4 Education on antimicrobial stewardship is part of postgraduate training of infectious diseases physicians, microbiologists, pharmacologists, nurses and pharmacists.

6.3 Education of prescribers

Major reasons for inappropriate antimicrobial prescribing include a lack of knowledge about infectious diseases (ID) and antimicrobial therapy, and a fear of not prescribing antimicrobials.[98] In the United Kingdom, poor prescribing has been linked to the lack of an integrated scientific and clinical knowledge base, and the absence of practical prescribing instructions for undergraduates.[99] With limited time to teach antimicrobial pharmacology and IDs in medical school curriculums, prescribers are said to acquire their antimicrobial prescribing habits from observing the practice of colleagues, recommendations in antimicrobial handbooks and information from representatives from the pharmaceutical industry.[12]

However, a clinician's decision to prescribe is not solely based on subjective beliefs or knowledge of evidence-based practice. Clinicians are influenced by a variety of factors relating to the healthcare system, and by the patient's beliefs and expectations.[100] Although most clinicians are aware of the problem of antimicrobial resistance, most underestimate the degree of resistance in their own hospital.[12] As their primary concern is with the effects of antimicrobials in individual patients, the risk of contributing to resistance ranks low among factors that influence the selection of an antimicrobial agent.[12]

Education is a cornerstone of antimicrobial stewardship (AMS) programs and integral to their success.[1, 12, 15-17, 23, 101]

Education is considered to be an essential element of any program designed to influence prescribing behaviour and can provide a foundation of knowledge that will enhance and increase acceptance of stewardship strategies.[1]

In this chapter, the evidence for the role of education in influencing the appropriate prescribing of antimicrobials is covered. Strategies shown to improve safe and judicious prescribing are discussed. Some examples of educational materials are provided in Appendix 2, Sections A2.1 and A2.3.

6.4 Educational strategies

Education is the most frequently employed intervention in programs designed to influence prescribing behaviour.[1] Activities can include formal lectures or tutorials, one-on-one education, discussions among ID physicians and treating clinicians at the bedside, or providing information over the telephone or via writing in medical notes.[102] However, education alone has been shown to be only marginally effective in changing prescribing practices and has not been shown to have a sustained effect.[1] Education is considered as a starting point for AMS programs, with more active interventions required to reinforce appropriate prescribing of antimicrobials. The Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America list education as a supplementary activity to the core active AMS strategies of formulary restriction and prospective review with intervention and feedback.[1]

Figure 6.1, adapted from the diagram developed by MacDougall and Polk,[12] depicts the antimicrobial prescribing process and the aspects towards which the different AMS strategies are directed. They describe education as influencing prescribing during the 'patient evaluation' and 'choice of antimicrobial' stages of the process.
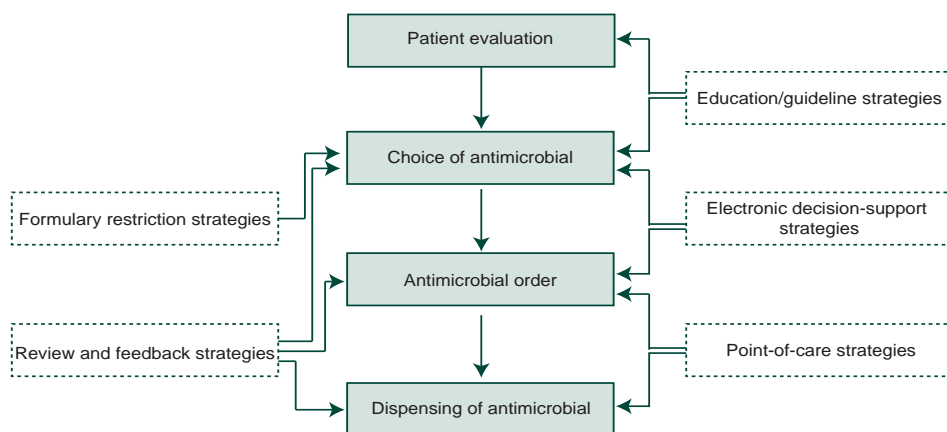
Source: Adapted with permission from MacDougall and Polk (2005)[12]

Figure 6.1   Antimicrobial prescribing process (solid boxes) and antimicrobial stewardship strategies (dotted boxes)

Education is considered a 'persuasive intervention', as distinct from a 'restrictive intervention' such as formulary restrictions or requirement for prior approval by ID physicians.

The education of prescribers is divided into passive and active strategies. Table 6.1 shows examples of passive and active education in the hospital setting. Active

personalised interventions have been shown to be more effective in changing prescribing behaviour than the passive dissemination of information.[1, 12, 34, 103]

Table 6.1   Examples of passive and active education strategies

Passive education strategies	Active education strategies
Printed prescribing guidelines	Consensus-building sessions
Posting national guidelines on the hospital web site	Workshops
Posters, printed handouts	Academic detailing
Attendances at conferences	
Minimally interactive sessions such as:	
• student or staff teaching sessions	
• medical teaching rounds	

Active education requires clinicians to interact and actively participate in their education in small groups (e.g. consensus-building sessions and workshops) or one-on-one sessions (e.g. academic detailing and educational outreach).[12, 103] Academic detailing is described as 'one-on-one educational sessions between an academic clinician educator (usually a physician or pharmacist) and the clinician targeted for education'.[12] These face-to-face educational visits have been shown to have far greater and more lasting effects on changing prescribing behaviour than printed material or group interactions alone.[104] The technique has been cited as probably the most effective single method for changing prescribing behaviour.[105] Indeed, the technique uses strategies that are employed by pharmaceutical industry representatives to influence prescribing behaviour.

Prescriber feedback — where prescribers are provided with data on their prescribing habits compared with hospital guidelines, or with other prescribers in the same field of practice — can be included as an active component of an education strategy. Prescriber feedback combined with academic detailing can be used on a general level or at a patient-specific level. An example of general use would be an ID physician supplying information on antimicrobial use on the haematology/oncology ward when discussing new guidelines for febrile neutropenia with an oncologist.[12] At an individual patient level, education can be provided as part of an intervention (e.g. during the approval process or feedback following review of antimicrobial prescribing). The use of prescriber feedback in influencing prescribing behaviour is discussed further in Chapter 3.

Active education strategies may include multifaceted interventions combining the formulation of consensus local guidelines with academic detailing and prescriber feedback.

6.5   The evidence that education influences prescribing

There have been numerous studies on persuasive and educative interventions to improve antimicrobial prescribing practices. The interventions have been made by pharmacists (see Chapter 9) or ID physicians (see Chapter 8), or both.

Active personalised interventions have been shown to be more effective than the passive dissemination of information.[1, 12, 34, 103] MacDougall and Polk describe three studies comparing the provision of printed educational material with more active methods, such as academic detailing. Improved adherence to guidelines were found in the active intervention groups.[12]

The Cochrane review of interventions to improve antimicrobial prescribing practices for hospital inpatients looked at 66 studies.[22] Sixty studies used persuasive and restrictive methods to reduce unnecessary antimicrobial use. Six studies tested methods to increase the use of antimicrobials to prevent infection (i.e. surgical prophylaxis around time of surgery). Persuasive methods included:

- active and passive education activities, such as

    » distribution of educational material

    » educational meetings

    » local consensus processes

    » academic detailing

    » use of local opinion leaders

- reminders (verbal, on paper or electronic)

- audit and feedback.

The primary outcome measure of the reported studies included one or more of the following: decision to prescribe, prescribing of recommended choice, and dosage or duration of therapy. In addition, 64% of persuasive single interventions and 75% of persuasive multifaceted interventions were considered successful. The information available from the studies does not allow any analysis of the sustained effect of the interventions.

In a publication on antimicrobial prescribing behaviour in the outpatient setting, the Agency for Healthcare Research and Quality evaluated 54 studies examining the effectiveness of quality improvement strategies targeting antimicrobial prescribing.[103] Educational approaches were subdivided into active strategies, where clinicians interacted and participated actively in their education in small groups or one-on-one sessions, and passive strategies where there was no active engagement in the learning process (e.g. lectures, distribution of educational materials). The authors concluded that active educational strategies appeared to be more effective than passive education, although this was not statistically significant. However, in the five studies comparing active and passive educational strategies, active strategies were shown to be superior in terms of reducing inappropriate prescribing and improving the selection of antimicrobials. Although this review was of studies in outpatient settings, conclusions about active education as an effective strategy in influencing prescribing behaviour are also relevant to the acute setting.

Programs combining surveillance, education, feedback and prescription controls have been shown to reduce the number of antimicrobial prescriptions, the level of antimicrobial use and costs.[81, 98] Bantar et al.[81] describe the implementation of

a four-step program to optimise antimicrobial usage in an intensive care unit. The introduction of an order form (phase 1) and feedback on data, including bacterial resistance, nosocomial infection, antimicrobial use and prescribing practice (phase 2) was followed by the education component (phase 3). Education included bedside discussion among ID physicians, a clinical microbiologist and attending physicians. This was aimed at documenting an infection microbiologically before commencing therapy, avoiding antimicrobials known to be associated with the emergence of resistant organisms and increasing the use of antimicrobials thought to reduce the frequency of emerging multiresistant organisms. Phase 4 was active control, with the AMS team modifying antimicrobial prescribing practice. After the education phase, there was a dramatic decrease in the intention to prescribe carbapenem (6.39% after phase 3 versus 13.54% at baseline) and ceftriaxone (26.63% versus 62.85%). Similarly, a program in a tertiary care hospital in Thailand that combined education and an antimicrobial control program demonstrated sustained reduction in antimicrobial use, significant reductions in the incidence of infections due to resistant organisms and cost savings.[106] These studies demonstrate the importance of including education in any AMS program.

6.6 Educational resources

This section describes educational resources (guidelines and web sites) that can be used as teaching tools and for practitioners to use to improve prescribing practice.

6.6.1 Guidelines

Evidence-based clinical guidelines are a popular educational tool for practitioners and have become a major feature of health care.[107] In a number of countries, including Australia, clinical guidelines have been produced and developed by a range of organisations.[105] The aim of clinical guidelines is to improve treatment outcomes through changing practitioner knowledge, attitudes and behaviour, such that their practice accords with guideline recommendations.[105]

The introduction of evidence-based guidelines for antimicrobial treatment and prophylaxis is considered to be a key element of any AMS program.[1, 12, 16, 18] This is supported by high-level evidence that multidisciplinary development of evidence-based practice guidelines incorporating local microbiology and resistance patterns can improve antimicrobial use.[1] Guidelines form the basis for educating prescribers on accepted practice for antimicrobial prescribing in the institution. The *Therapeutic Guidelines: Antibiotic*[19] are recognised as a national standard for antimicrobial prescribing in Australia,[2] and institutional clinical guidelines developed for local use should reflect the nationally agreed practice contained in these guidelines. Prescribers should be taught to follow these guidelines and to seek expert guidance from ID specialists and pharmacists in situations not covered by the guidelines. Guideline development and implementation are further discussed in Chapter 8.

Increased adherence to best practice guidelines should be a major objective of AMS programs. Key activities should include auditing the level of compliance of antimicrobial treatment with guidelines and formulary recommendations, and providing feedback to

prescribers and clinical departments. See Chapters 3 and 5 for further discussion on the use of audit to monitor and provide feedback on antimicrobial use.

6.6.2   Guideline implementation

Numerous studies have shown poor uptake of guideline recommendations.[107] To be effective, guidelines need well-developed implementation plans that are well executed, sustained and embedded in comprehensive programs for change.

There is evidence that guideline implementation can be facilitated through education and feedback on antimicrobial use and patient outcomes.[1]

In teaching hospitals, where senior medical clinicians influence trainees' prescribing, ensuring that senior staff 'buy in' to the process through involvement in local guideline development is considered particularly important. Aiming education at authoritative senior department staff has been shown to have a significant impact in changing surgical antimicrobial prophylaxis practices.[12]

The lack of awareness among senior clinicians and registrars of local and national resources available to support decision making has been identified as a barrier to appropriate prescribing.[99] The AMS team can play an important role in promoting the existence of antimicrobial prescribing guidelines and making them readily available. See Chapter 8 for further details on guideline implementation.

6.6.3   Web sites

Establishing an up-to-date web site on the institution's intranet (or on the internet) has been proposed as an excellent way for an institution to provide easy access to information on their AMS program and current strategies.[3] Ideally, such web sites would be publicly available; facilitating the sharing of ideas, and possibly helping other hospitals to implement similar programs.[3, 108] Pagani et al. have published a review of web sites containing resources on antimicrobial stewardship.[108] Examples of antimicrobial stewardship web sites they cite as providing useful starting points for designing and implementing antimicrobial stewardship programs are:

- national organisation web sites

    » Healthcare Infection Control Special Interest Group
      www.asid.net.au/hicsigwiki — an Australian and New Zealand site that provides a good example of multidisciplinary AMS and contains helpful information, teaching materials and a large number of related links

    » Centers for Disease Control and Prevention
      www.cdc.gov/drugresistance — contains teaching material and valuable tools to download, including '12 steps to prevent antimicrobial resistance amongst hospitalized adults'

- institutional web sites

  » Nebraska Medical Center
    www.nebraskamed.com/asp — provides information about
    different aspects of an institutional AMS program

  » the 'Antibiotic Management Program' of the University of
    Pennsylvania Health System
    www.uphs.upenn.edu/bugdrug — covers many aspects of
    AMS, including guidelines for antimicrobial therapy, issues
    relating to formulary restrictions and pharmacologic
    considerations for dose adjustments.

Additional information on AMS web sites is available in Appendix 2,
Section A2.

6.7   Education programs

A firm educational grounding for undergraduates, consolidated
with further training throughout the postgraduate years, has been
recommended to achieve appropriate and prudent prescribing of
antimicrobial agents.[17]

Educational programs should emphasise the principles of judicious,
safe and effective antimicrobial prescribing and the concept of
resistance.[17, 102] Factors influencing prescribing, including the effect
of promotional activities conducted by the pharmaceutical industry,
should be addressed (see Section 6.8). Because active education is
more effective in changing prescribing behaviour, the educational
component of AMS programs should include interactive group
sessions and one-on-one educational strategies, such as academic
detailing and the use of audit and prescriber feedback.[1, 12, 34, 100]

The Scottish Medicines Consortium Short Life Working Group and
the Scottish Executive Health Department Healthcare Associated
Infection Task Force have developed a set of good practice
recommendations for antimicrobial prescribing in hospitals.[17]
Key area 2 of the paper by Nathwani[17] covers the structures and
responsibilities for multidisciplinary and generic undergraduate
and postgraduate training relating to antimicrobial prescribing. The
author lists four recommendations that cover:

- competencies and skills for prudent prescribing defined by
  the institution's AMS team, based on national models (where
  appropriate)

- a structured, competency-based, multidisciplinary postgraduate
  teaching program for professionals involved in prescribing and the

*Each country and
region should have
an educational
programme for
patients, health care
professionals and
students to reduce
patient pressure
on doctors to
prescribe antibiotics
and educate
medical students
and all health
care professionals
on good quality
antibiotic prescribing
and responsible use
of antibiotics.[16]*

administration of antimicrobials, with regular repetition to cover the frequency of job changes in this group of prescribers

- assessment of competency to prescribe and documentation of education in a continuing education portfolio (in the United Kingdom, National Health Service [NHS] healthcare workers are required to attend specific healthcare associated infection-related continuing professional development activities)

- consideration by deans of curriculums to consider outcomes of undergraduate education on prudent antimicrobial prescribing.

6.7.1 Undergraduate education

There is evidence that many medical students are not trained adequately in pharmacotherapy and training programs do not adequately equip the future prescriber with the fundamentals required for optimal antimicrobial prescribing.[15, 105] In the United Kingdom, poor antimicrobial prescribing has been linked with a lack of an integrated scientific and clinical knowledge base, and an absence of practical prescribing instructions for undergraduates.[99] The limited time available to teach antimicrobial pharmacology and IDs in medical school curriculums is given as the reason that prescribers often acquire their antimicrobial prescribing habits from the practice of colleagues, recommendations in antimicrobial handbooks and information from representatives from the pharmaceutical industry.[12]

A sound undergraduate education in IDs and antimicrobial therapy is a requirement for achieving safe and appropriate prescribing of antimicrobial agents.[17] Marwick and Nathwani[99] describe an outcomes-based internet program (Appropriate Antimicrobial Prescribing for Tomorrow's Doctors; APT) for teaching and reflective learning of antimicrobial prescribing. The program was developed by the Scottish medical schools and the British Society for Antimicrobial Chemotherapy. It has been adopted by medical schools throughout the United Kingdom and is available from the Prudent Antibiotic User (PAUSE) web site.[a] The web site provides shared, standardised teaching materials on prudent antimicrobial prescribing for use by educators teaching undergraduate medical curriculums.

6.7.2 Postgraduate education

Equally important is the need for postgraduate medical and nonmedical prescribers (nurses, pharmacists, dentists, etc) to develop the skills and attitudes that will allow them to prescribe antimicrobials safely and effectively. The availability of appropriate training programs for all prescribers has been recommended in the United Kingdom in the NHS's *Saving Lives: Reducing Infection, Delivering Clean and Safe Care*[18] (an antimicrobial prescribing summary of best practice).

At the level of the hospital, education should be provided early in prescribers' employment, such as during initial orientation. Staff education and development

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a   www.pause-online.org.uk

should include the institution's antimicrobial guidelines and policies for antimicrobial prescribing.[17, 24] Programs should be structured and competency based, and sessions repeated regularly to take into account changes in junior medical staff rosters.[17]

Education about the purpose of AMS and details about the functions of a program, including the availability of institutional guidelines, should not be overlooked.[3] Understanding the context in which recommendations are made will reduce delays in therapy caused by ordering a restricted drug without approval.[3] The fears of those clinicians who are concerned about the risks of not treating or undertreating infected patients, and possible adverse consequences of stewardship interventions, can be allayed by highlighting published reports that illustrate the safety of risk stratification, streamlining broad-spectrum therapy, intravenous-to-oral conversions and reducing the duration of therapy.[3]

As all doctors prescribe antibiotics, good quality antibiotic prescribing should be part of all doctors' continuous professional development, accreditation and clinical governance programmes. [16]

6.7.3 e-learning programs

The APT program has been adapted to provide online training and assessment for junior medical officers working in Scottish hospitals.[99, 109] The program reinforces the principles and practices taught at the undergraduate level and encompasses a range of competencies and learning outcomes. Enrolment in the program is mandatory for new prescribers in Scottish hospitals. The authors report that at any given time more than 1600 junior medical staff undertake the mandatory exercise and demonstrate evidence of satisfactory completion.

The Central Manchester University Hospitals Trust is developing an e-learning package on antimicrobial prescribing. The package comprises three modules: principles of antimicrobial management, hospital acquired infection and antimicrobial medication safety (Table 6.2). The package will include a bank of multiple-choice questions and an assessment facility. The package is aimed at all grades of prescriber for adult and children's specialties.

Table 6.2   Content of e-learning package, Central Manchester University Hospitals Trust

Module	Content
1 Principles of antimicrobial management	Rationale for prudent use Antimicrobial formulary Intravenous-to-oral switch De-escalation and antimicrobial spectrum Surgical prophylaxis
2 Hospital acquired infection	Methicillin-resistant *Staphylococcus aureus* *Clostridium difficile*
3 Antimicrobial medication safety	Antimicrobial allergy Vancomycin monitoring Aminoglycoside monitoring

6.8   The influence of the pharmaceutical industry

This section reviews the effects of the pharmaceutical industry on the prescribing of medicines. It highlights the importance of including education about the influence of pharmaceutical industry relationships and sponsorship on prescribing behaviour in training programs for new prescribers.

Published literature reviews[110-112] studying the effects of interactions between medical professionals and the pharmaceutical industry confirm that these interactions can:

- increase formulary addition requests, even when there is no therapeutic advantage over existing formulary drugs

- affect prescribing practices, including prescribing costs, nonrational prescribing, a preference for new drugs and the decreased prescribing of generic drugs.

Prescribers often deny that gifts may influence their behaviour and are equivocal about the ethics of such a practice.[110-112] However, receiving a gift, and the number of gifts, correlated with the belief that interactions with pharmaceutical representatives have no impact on prescribing behaviour. In addition, most prescribers admitted that without gifts their interactions with pharmaceutical representatives would be reduced. Samples, continuing medical education and conference travel funding, exerted more influence than promotional material. Payments for travel generated the most ethical concerns.[110-111] Table 6.3 lists the influence of gifts on prescribing behaviour derived from the Wazana literature review.[111]

The Zipkin review of interactions between pharmaceutical representatives and trainee doctors reported frequent involvement of pharmaceutical representatives in training programs.[112] Activities described included:

- 'detailing' products

- sponsoring conference attendance, presentations and food

- providing cash support for social activities.

Zipkin reported residents' attitudes to the pharmaceutical industry as largely positive. They believed themselves to be more immune to industry influence than their colleagues. Most felt that the receipt of gifts did not influence their behaviour. Those residents in programs with regulatory policies had a more sceptical approach. There was a significant association between company sales visits and the prescription of company product.[112]

These reviews all confirm a temporal association between:

- an increase in industry-sponsored continuing medical education and the physician prescribing rate of the sponsor's drug

- an increase in travel sponsorship and hospital prescribing of the travel sponsor's drug

- an increase in nonrational prescribing of a sponsored drug after teaching delivered by pharmaceutical representatives.

Table 6.3   Influence of gifts from pharmaceutical industry on prescribing behaviour

Description of gift	Influence on prescribing behaviour
Samples	Accepting samples is associated with awareness, preference and rapid prescription of a new drug
Industry-paid meal	There is an association between accepting sponsored meals and formulary addition requests
Funding for travel	Accepting funding is independently associated with increased formulary addition requests for the sponsor's drug
Pharmaceutical representative speakers	Speakers are associated with inaccurate information about sponsors' and competitors' drugs, and inappropriate treatment decisions
Honoraria, research funding	Honoraria and research funding are associated with formulary addition requests for the sponsor's drug

Involvement in the conduct of clinical trials sponsored by pharmaceutical companies has also been shown to influence prescribing.[110, 113] Andersen et al. found that conducting a trial sponsored by a pharmaceutical company had no significant impact on a physician's adherence to international treatment recommendations, but increased the use of the trial sponsor's drugs.[113] Wazana et al. identified a significant association between the outcome of the study and the source of funding (i.e. pharmaceutical-funded studies were much more likely to favour new therapies) and a suggested association between source of funding and trial design (e.g. a new non-steroidal anti-inflammatory drug [NSAID] was more likely to be compared with other NSAIDs than with a pure analgesic drug).[111]

These studies illustrate some apparent incongruities between doctors' attitudes and beliefs, and their behaviour. Doctors do not believe that their behaviour will be influenced by interaction with the pharmaceutical industry (although they believed that their colleagues may be), yet studies have repeatedly shown an association between interaction and prescribing behaviours. Doctors also have a negative attitude towards physician–industry interaction (e.g. poor-quality information or ethical issues), yet most continue to participate.

The dynamics of the relationships between physicians and pharmaceutical company representatives was explored by Chimonas et al.[114] They analysed the contradiction of physicians' awareness of the negative effects of detailing and their approval of the relationships, and explored the policy implications. They applied the concept of 'cognitive dissonance'[115] to the relationship between physicians and pharmaceutical company representatives. Cognitive dissonance is described as a preference for one's beliefs to be consistent with each other. When cognitions are dissonant, people experience discomfort and attempt to reduce the dissonance. Cognitive dissonance can be managed by:

• elimination of the dissonance, by altering one or more of the conflicting attitudes or behaviours

- rationalisation, by using additional information to reduce dissonance between conflicting cognitions

- denial, by forgetting or rejecting the significance of one or more of the conflicting elements.

In Chimonas et al., the 32 academic and community physicians participating in focus groups held in three cities in the United States acknowledged and recognised the conflict of interest, but expressed irritation at regulatory efforts to address the conflict, especially limitations on entertainment and personal-use gifts. The authors concluded: 'Given physicians' techniques for managing dissonance, it appears that only the prohibition of physician–detailer interactions will be effective'.

6.8.1 Solutions for reducing the influence of the pharmaceutical industry

A variety of solutions have been proposed for reducing the influence of the pharmaceutical industry on the prescribing of antimicrobials, including:

- education and training beginning at medical student level

- 'academic detailing' delivered by pharmacists, as described in Section 6.4 and Chapter 9

- industry-independent drug information (e.g. pharmacy bulletins, mail-outs)

- the introduction of hospital policies to restrict pharmaceutical representatives' access to staff

- the development of guidelines on duality of interest (conflict of interest) by professional societies and colleges, and their incorporation into hospital policy and training programs.

Such guidelines have been developed by some state and territory health departments, often including a register of gifts and payments to healthcare providers and departments, or alternatively banning all gifts. Medicines Australia, the pharmaceutical industry's national association, has a voluntary self-regulatory code and publishes an educational event report annually on its web site. (See Appendix 2, Section A2.2 for examples of guidelines, codes of conduct and position statements.)

Part 2

Resources required for antimicrobial stewardship

7 The role of the clinical microbiology service

Author: John Ferguson

7.1 Key points

- The clinical microbiology service is an essential and integral part of organisational initiatives that underpin antimicrobial stewardship efforts.

- The establishment of best practice procedures for rapid microbiological evaluation is critical to delivering timely and accurate information.

- Intensive care units are an area of particular importance, as the control of resistance in these units can affect other areas of the hospital. The clinical microbiology service should therefore pay particular attention to services provided to these areas.

- Reports to the clinician from the clinical microbiology service can provide comments that interpret isolate significance, provide antimicrobial susceptibility interpretation and provide antimicrobial management advice.

- The clinical microbiology service also has a critical role to play in improving overall antimicrobial use through providing information, establishing guidelines and educating other hospital staff. One key strategy is the production of annual cumulative antibiograms to indicate susceptibility patterns for key pathogens.

- The clinical microbiology service provides surveillance data on resistant organisms for infection control purposes.

7.2 Recommendations

! 7.2.1 Hospitals have access to a clinical microbiology service that provides:

» best practice diagnostic testing for infection, including relevant rapid tests for common viral, fungal or bacterial pathogens that are reported to clinicians

» consultation on choice, nature, handling and testing of specimens for detection of infection, especially when there is a broad infectious differential diagnosis under consideration

» direct advice from a specialist consultant or supervised registrar to clinicians at the time when bloodstream, meningeal or other critical infection is detected (this should occur seven days per week)

» regular patient-specific liaison with clinicians (including infectious diseases physicians if they are not integrated with the clinical microbiology service) who care for patients at a high risk of infection (e.g. patients in intensive care, haematology and oncology units).

7.2.2 Regular analyses of antimicrobial resistance are provided to groups with responsibility for local antimicrobial guidelines (e.g. antimicrobial stewardship committee, drug and therapeutics committee) to inform local empirical therapy recommendations and formulary management.

7.2.3 Cascade reporting of antimicrobial susceptibility is consistent with the *Therapeutic Guidelines: Antibiotic.*[19]

7.2.4 A national standard approach to antimicrobial susceptibility testing and cumulative analysis and reporting of antibiograms is developed, agreed and implemented by clinical microbiology services.

7.3 Clinical microbiology services' involvement in antimicrobial stewardship

The clinical microbiology service (CMS) is an essential and integral part of a wide range of organisational initiatives that underpin antimicrobial stewardship (AMS) efforts. At some sites, many of these activities are done in conjunction with infectious diseases consultants and registrars. The CMS supports the clinician with data to inform individual patient diagnosis and treatment decisions, and should provide leadership in developing and maintaining best practice in the organisation's antimicrobial use.

The CMS participates in a range of organisational AMS activities.[116] These include:

- preparation of antimicrobial susceptibility reports (see Section 7.5)
- participation in
  - » quality use of medicine, and drug and therapeutics committees (formulary controls, reporting on antimicrobial use)
  - » evaluation and reporting of hospital antimicrobial use in conjunction with pharmacists
  - » development, review and audit of clinical pathways or guidelines for common disorders (e.g. pneumonia) to ensure that optimal practices of investigation are specified
  - » surveillance of healthcare associated infections, especially facilitating classification of the healthcare association status of bloodstream infections
- liaison with infection prevention and control staff and, where possible, promoting and supporting their safe practice agenda
- conducting antimicrobial education of medical staff, pharmacists and other clinical staff.

For a more detailed summary of clinical microbiology roles and the recommended processes, see the Healthcare Infection Control Special Interest Group web site.[a]

7.4 Diagnostic testing practice

A specific microbiological diagnosis enables effective targeting of antimicrobial therapy against demonstrated pathogens. Microbiological results may allow an early decision to shift to directed treatment or cessation of antimicrobials, reducing unnecessary exposure.

7.4.1 Specimen collection

The CMS should promote the optimal microbiological evaluation of patients prior to commencing antimicrobials. The service should establish procedures for microbiological and related specimen collection according to best practice

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a www.asid.net.au/hicsigwiki/index.php?title=Category:Antibiotics

guidelines, and incorporate them into AMS education activities.[12] Some of the more important issues are outlined below:

- Blood culture collection techniques that avoid contamination and ensure adequate sensitivity of detection, such as

  » avoiding contamination through use of appropriate antisepsis during collection (see Table 7.1)

  » avoiding collecting cultures via pre-existing central or peripheral lines — use of pre-existing lines reduces the specificity of a positive result and places the line at risk of contamination, which may cause subsequent line-related healthcare associated infection

  » collecting at least two blood culture sets in an adult from separate venipunctures — this helps to achieve acceptable sensitivity and enables confirmation of infection due to organisms that may potentially contaminate blood cultures.

- Urine specimen collection that avoids contamination or nonspecific results. Common problems that reduce specificity of the result include collection of urine

  » via old indwelling catheters

  » from asymptomatic patients (unless required for pre-operative or antenatal demonstration of significant bacteriuria).

- Collection of specimens for demonstration of viral infection when relevant.

- Performance of additional tests relevant to particular clinical syndromes (e.g. *Legionella pneumophila* urinary antigen testing or nucleic acid amplification test for *Neisseria meningitidis* from blood or cerebrospinal fluid, *Legionella* species from sputum).

- Appropriate use of acute-phase reactants (e.g. C-reactive protein, procalcitonin) to help rule in or rule out microbial sepsis.

The CMS needs to provide education to clinicians about specimen collection and laboratory testing procedures. Periodic summaries of blood culture contamination rates and analyses of organisms detected in particular specimen types provide useful feedback that can help modify practice.

The clinical microbiology laboratory plays a critical role in antimicrobial stewardship by providing patient specific culture and susceptibility data to optimize individual antimicrobial management and by assisting infection control efforts in the surveillance of resistant organisms and in the molecular epidemiologic investigation of outbreaks.[1]

7.4.2 Microbiology testing practice

The CMS should implement best practice methods for organism identification and determination of antimicrobial susceptibility.

Adequate analytical performance (e.g. for detection of susceptibility) should be demonstrated through performance in external quality-assurance programs.

7.4.3 Rapid testing

Many technologies are now available to enable rapid (same-day) analysis of specimens to either rule out or rule in infection. The availability of valid rapid results enables quicker streamlining of antimicrobial therapy. Examples of useful rapid tests include:

- direct nucleic acid amplification tests for
    - » viruses (e.g. influenza from respiratory samples, cytomegalovirus from blood)
    - » bacteria (e.g. *Neisseria meningitidis* from blood or cerebrospinal fluid)
    - » methicillin-resistant *Staphylococcus aureus* from infection control screening swabs
    - » fungi or bacteria (e.g. from sterile site tissue samples)
- direct antigen detection tests from
    - » blood (e.g. *Cryptococcus neoformans*)
    - » respiratory samples (e.g. respiratory syncytial virus, influenza)
    - » faeces (e.g. *Clostridium difficile*, rotavirus, norovirus)
    - » urine (e.g. *L. pneumophila, Streptococcus pneumoniae*)
    - » cerebrospinal fluid (e.g. *C. neoformans, S. pneumoniae*)
- acute serological tests to demonstrate organism-specific IgM (e.g. measles, rubella diagnosis)
- secondary rapid tests performed on
    - » positive blood culture broth samples (e.g. Gram staining, direct coagulase testing to demonstrate presence of *S. aureus*, nucleic acid amplification to demonstrate *S. aureus* and methicillin resistance, other modalities (e.g. protein–nucleic acid fluorescent in situ hybridisation probes)
    - » bacterial or viral isolates from samples to confirm identification.

7.5 Microbiology reporting practice

The CMS should use cascade (also known as selective) reporting of antimicrobial susceptibilities.[1, 12, 16] Cascade reporting involves a process of reporting antimicrobial susceptibility test results whereby secondary agents (i.e. those that are more broad spectrum) may only be reported if an organism is resistant to primary agents within a particular drug class.[117] Routine reporting of susceptibility to nonformulary or restricted antimicrobial agents should be avoided.[17]

Microbiology reports should also include a range of comments to help clinicians distinguish infection from contamination or colonisation (i.e. antimicrobial therapy is therefore not required). Example comments are provided in Table 7.1.

Table 7.1   Example microbiology report comments that interpret isolate significance

Specimen type	Indication	Reporting comment
Blood	Isolate of CoNS from ICU patient — mixed or isolated after prolonged incubation (> 1 day), only one set taken	For optimal sensitivity and specificity, at least two separate blood culture sets (adult, 20 mL each) should be collected from separate venipuncture sites prior to beginning antimicrobial treatment. This patient had one set collected and has an isolated CoNS. This result is consistent with either infection or contamination — clinical correlation is required.
Blood	Isolate of potential contaminant organism(s) from non-ICU patient — mixed or isolated after prolonged incubation (> 1 day), not present in multiple sets	This isolate most likely represents contamination. To avoid contamination during blood culture collection, ensure: • collection is not done through pre-existing or new intravascular lines • hand hygiene is performed with alcohol-based hand rub prior to procedure, and wear protective eyewear • the skin site and blood culture bottle caps are disinfected with alcohol (applied for at least 1 minute) • sterile gloves and the no-touch technique for venipuncture are used • needle exchange prior to inoculation of bottle(s) is avoided.
Faeces	Isolate of *Campylobacter*	*Campylobacter* gastroenteritis does not normally require antimicrobial treatment. However, in severe or prolonged cases and during pregnancy, erythromycin is recommended.
Mucosal or skin site swab	Gram stain or culture (or both) shows presence of nonpathogenic micro-organisms	Gram stain or culture (or both) result is consistent with normal flora.
Nonsterile site isolate	Antimicrobial susceptibility reported for information rather than to recommend treatment	The reporting of antimicrobial susceptibility does not imply that treatment with antimicrobials is necessary. Colonisation (as opposed to infection) does not require antimicrobial treatment.

CoNS = coagulase-negative staphylococci; ICU = intensive care unit

Laboratories should make local sensitivity patterns widely known and routinely should only report on those agents which appear in their formulary and policy.[16]

Comments that assist the interpretation of antimicrobial susceptibility should also be included. Example comments of this type are in Table 7.2.

Table 7.2   Example microbiology report comments that provide antimicrobial susceptibility interpretation

Specimen type	Indication	Reporting comment
Any site	Penicillin-resistant, methicillin-sensitive *Staphylococcus aureus* OR Beta-lactamase-negative *S. aureus*	*S. aureus* susceptible to flucloxacillin or dicloxacillin is also susceptible to cephazolin, cephalexin, and amoxycillin with clavulanate. Penicillin-susceptible strains can be treated with benzylpenicillin or amoxycillin. Cephazolin or cephalothin are suitable alternatives in the penicillin-allergic patient, unless the penicillin allergy is of the severe immediate type, in which case all beta-lactams should be avoided.
Any site	*S. aureus* sensitive to erythromycin	The erythromycin result can be used to predict clindamycin and lincomycin susceptibility.
Any site	*Eikenella corrodens* isolate	*Eikenella corrodens* is an aerobic, oral, gram-negative organism. Most isolates are susceptible to benzylpenicillin, amoxycillin and tetracyclines. They are resistant to di/flucloxacillin, erythromycin and aminoglycosides.[*]
Respiratory tract	*Streptococcus pneumoniae* with penicillin minimum inhibitory concentration of ≤ 2 mg/L	Penicillin-susceptible isolates of *S. pneumoniae* are susceptible to amoxycillin.

* This is an example of an organism that is not tested routinely. The CMS provides advice based on published literature to guide the clinician's choice of therapy.

Comments that provide specific directed treatment advice are an important way of helping clinicians to direct antimicrobial therapy appropriately and to advise them of relevant treatment guidelines (national and local). Reporting and telephone liaison should promote compliance with *Therapeutic Guidelines: Antibiotic*[19] wherever possible. Table 7.3 provides examples of this sort.

Reporting of microbiology susceptibility test results should be timely and accurate. This allows selection of more appropriate and focused therapy, and may help reduce broad-spectrum antimicrobial use.[12, 20]

For critical microbiology results (e.g. a penicillin-resistant isolate of *S. pneumoniae* in a patient with meningitis), it is essential that urgent discussion with the clinician takes place so that appropriate treatment is not delayed.

Table 7.3   Example microbiology report comments that provide antimicrobial management advice

Specimen type	Indication	Reporting comment
CSF or blood in meningitis patient	*Streptococcus pneumoniae* (MIC PEN ≥ 0.12 mg/L)	Significant level of penicillin resistance is present. Alternative therapy needs to be considered. Please discuss with the clinical microbiologist [*in reality, such a result should prompt an urgent telephone consultation*]. (This is a CLSI-based MIC interpretation — some laboratories use other methods and resistance breakpoints.)
Blood	*Staphylococcus aureus* isolate	Prolonged IV treatment is indicated, preferably via a peripherally inserted central line. Relapse of *S. aureus* bacteraemia occurs in up to 5% of patients and may present up to 3 months following the event. Patients should receive education to this effect.
Blood	*S. pneumoniae* (MIC PEN > 2 mg/L, ≤ 4 mg/L)	This isolate demonstrates reduced susceptibility to penicillin. Benzylpenicillin at a dose of 50 mg/kg up to 1.8 g IV 4-hourly remains satisfactory therapy for infections other than meningitis due to this organism. (This is a CLSI-based MIC interpretation — some laboratories use other methods and breakpoints.)
Pus or wound swab	*S. aureus* isolate from patient with history of boils	If an undrained skin or soft tissue infection is present, early incision/drainage may be curative. If lesion is larger than 5 cm in diameter, also treat with one of the indicated oral antibiotics. AVOID monotherapy with rifampicin. If systemic sepsis is present, collect blood cultures and either use IV flucloxacillin (for MSSA) or vancomycin (for MRSA) for initial treatment. For recurrent staphylococcal infections, refer to [*insert information resource link*].
Pus or wound swab	Cellulitis patient with isolates of *Streptococcus pyogenes* or other beta-haemolytic streptococci, or MSSA	Monotherapy for cellulitis with flucloxacillin or dicloxacillin is effective in most patients. For a more complete discussion of this topic, refer to [*insert information resource link*].

Susceptibility and culture results should be reported to clinicians with minimum of delay to allow them to streamline or stop antibiotic therapy as appropriate.[16]

Table 7.3 Example microbiology report comments that provide antimicrobial management advice *continued*

Specimen type	Indication	Reporting comment
Pus or sterile site aspirate, or tissue culture	Anaerobic isolates	Agents that are predictably active against gram-negative anaerobes (such as *Bacteroides* and *Prevotella* spp.) include metronidazole (12-hourly dosage recommended), lincomycin, clindamycin, amoxycillin/clavulanate, piperacillin/tazobactam, or ticarcillin/clavulanate. [*modify as per local formulary*]
Any site other than urine	MRSA	If initial systemic treatment is required, use IV vancomycin (see *Therapeutic Guidelines: Antibiotic*[19] for dosing advice). For uncomplicated skin or soft tissue infection, use one of the indicated oral antibiotics. AVOID monotherapy with rifampicin. For complicated or bone and joint infection, consult ID service.

CLSI = Clinical and Laboratory Standards Institute; CSF = cerebrospinal fluid; ESBL = extended spectrum beta-lactamase; ID = infectious diseases; IV = intravenous; MIC = minimum inhibitory concentration; MRSA = methicillin-resistant *Staphylococcus aureus*; MSSA = methicillin-sensitive *Staphylococcus aureus*; PEN = penicillin

7.6   Clinician liaison

The CMS provides key patient-specific information to the clinician. Liaison about results enables timely advice about appropriate empirical therapy (e.g. choice of agent, dose, route and duration). For critical results (e.g. blood or sterile site isolates), such liaison is best performed directly by telephone contact from a clinical microbiologist who may be located off-site.[a]

7.6.1   Intensive care antimicrobial liaison

A particular area of importance for effective AMS is the intensive care unit (ICU). Controlling resistance selection within intensive care has spillover effects for non-ICU patients.

Clinicians and ICU managers, in consultation with the microbiology service, need to regularly review antimicrobial use, changes in the ICU antibiograms (see Section 7.8) and multiresistant organism reports for the unit. This can provide the impetus to change local antimicrobial recommendations, with reference to *Therapeutic Guidelines: Antibiotic*,[19] and promotes adherence to relevant infection prevention and control measures.

A representative of the CMS should attend intensive care liaison rounds, which may be on a daily, twice-weekly or weekly basis, dependent on the size and case load

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a It is acknowledged that some rural microbiology services in Australia are not directly supervised by a clinical microbiologist. In that case, it is essential that microbiology diagnostic processes and reporting are regularly reviewed by an external clinical microbiology consultant.

of the particular unit. Most locations conduct these rounds in conjunction with an infectious diseases physician. Prior to or during the round, the CMS should review all recent microbiology from all current ICU patients. Liaison rounds involve:

- discussing each patient (appraising clinical presentation, prior treatment, current status)

- determining the function of treatment — whether prophylaxis, empirical or directed treatment

- interpreting existing microbiological results and recommending additional investigations if required to clarify the infection status

- recommending changes (in the light of patient situation, microbiology and guidelines) to

  » documented diagnosis

  » switch to directed treatment

  » defined or agreed duration of treatment, or later date for further review.

7.6.2   Haematology and oncology liaison

The CMS should provide a similar (weekly) liaison service to haematology and oncology departments. This will facilitate more effective use of microbiological testing, interpretation of test results and antimicrobial use in the high-risk inpatients managed by these services.

7.7   Antimicrobial level monitoring and review

The CMS should cooperate with clinical chemistry and pharmacy units to monitor submitted antimicrobial levels for results that are either above or below targets (e.g. aminoglycosides, vancomycin, antifungal agents).

Interpretative comments consistent with *Therapeutic Guidelines: Antibiotic*[19] should be appended to these reports. Where necessary, antimicrobial-level results may prompt contact with the clinician to discuss antimicrobial management. The CMS should facilitate access to antimicrobial-level data by pharmacy and other auditors to enable assessment of indicators that evaluate quality of use (see Chapter 5). Examples of quality indicators that are relevant for aminoglycosides[95] and glycopeptides have been published and should be considered for adoption.[77, 87]

7.8   Antimicrobial resistance analysis and reporting

Most CMSs produce antimicrobial susceptibility tables (antibiograms), which are used by clinicians to inform empirical antimicrobial choice (Figure 7.1). These may be made available on the hospital's intranet or on printed cards.[12] Ideally, all CMSs should provide analyses (at least annually) of antimicrobial resistance to both individual clinicians and to groups with responsibility for local antimicrobial therapy guidelines (e.g. the AMS committee, drug and therapeutics committee, or quality

use of medicines committee) to inform local empirical therapy recommendations and formulary management.[12, 17] A clinical microbiologist needs to interpret the antibiograms to recognise at which point an antimicrobial is no longer a reliable empirical agent against an organism or group of organisms.

The Clinical and Laboratory Standards Institute guideline M39-A2[118, a] is an accepted international standard for analysis and presentation of antibiograms. The methods in this document have not received full discussion in Australia and it has not yet been widely accepted as a local standard. As a matter of priority, a national standard approach to analysis and reporting of cumulative antibiograms should be developed, agreed and implemented across CMSs.

WHONET software[b] is one product that can process antimicrobial resistance data uploads from pathology information technology systems and produce cumulative antibiograms. This is often a challenging area for pathology organisations and warrants a national process to facilitate the information technology aspects of cumulative data analysis. CMSs that are struggling with unfriendly epidemiological data systems should focus on producing cumulative antibiograms for clinical areas such as emergency, intensive care, oncology or haematology in the first instance, as failure of empirical antimicrobial choice incurs the highest patient risk in these settings.

Trends in resistance for different organisms should be graphically visualised. Time series data on antimicrobial resistance are valuable for statistical correlation with antimicrobial use time series data. These analyses can identify significant antimicrobial use factors that are responsible for driving subsequent changes in the incidence of antimicrobial-resistant isolates within the hospital. Such data then can inform formulary decisions and antimicrobial use recommendations for particular clinical units (see Chapter 5 and Appendix 1 for more detailed information on use of time series analysis).

Analysis and reporting of relevant molecular resistance mechanisms (e.g. presence of carbapenemase or extended spectrum beta-lactamase enzymes within gram-negative organisms) or epidemiological markers (e.g. using one of many typing systems that are able to demonstrate significant clonality) provides additional descriptions of important endemic or emerging resistant pathogen epidemiology. These data can further inform AMS, and infection prevention and control strategies by identifying outbreaks and the dynamics of clonal pathogen transmission. Where relevant, participation of the CMS in existing targeted national surveillance programs (e.g. National Neisseria Reference network,[c] Australian Group on Antimicrobial Resistance[d]) may complement this process, providing access to detailed typing and molecular analysis of local microbial isolates.

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a   www.clsi.org

b   www.who.int/drugresistance/whonetsoftware/en/index.html

c   j.tapsall@unsw.edu.au

d   www.agargroup.org

Gram-positive	No. of isolates	Penicillin	Ampicillin*	Erythromycin	Methicillin*	Vancoymycin	Ceftriaxone			
Staphylococcus aureus	322		●	●	●	▲				
Coagulase negative staph	107		●		●	▲				
Enterococcus	172		◆			▲				
Strep pneumonia#	12	◆		◆	◆	▲	▲			

Gram-negative	No. of isolates	Ampicillin*	Gentamycin	Cephalothin**	Cefriaxone***	Ceftazidime	Piperacillin-tazo	Cotrimoxazole	Imipenem ❖	Ciprofloxacin
Escherichia coli	456	●	▲	●	▲		▲		▲	▲
Klebsiella spp.	127		▲	◆	▲		▲		▲	▲
Haemophilus influenzae	42	◆			▲					▲
Stentrophomonas maltophilia	21				●	●	●	▲		●
Pseudomonas spp.	124		▲			◆	▲		◆	◆
Acinetobacter spp.◊	17		▲				◆		▲	▲
Enterobacter spp.◊	86		▲				◆		▲	▲
Proteus mirabilis	55	◆	▲	◆	▲		▲		▲	▲
Serratia spp.◊	22		▲				▲		▲	▲
Citrobacter spp.◊	33		▲				◆		▲	▲
Morganella morganii◊	30		▲				▲		▲	▲

▲ > 90% effective
◆ 70–89% sensitive
● < 70% effective
blank cells = not reported

Strep pneumonia 73% fully sensitive, 18% intermediate
* Amoxycillin provides similar cover
*** Cefotaxime provides similar cover
** Cephazolin provides similar cover
❖ Meropenem provides similar cover
◊ Don't use cephalosporins, even if reported sensitive

XXX Hospital
Antibiotic sensitivity profile
Data from 1/1/200X to 31/3/200X
Whole Hospital

Figure 7.1   Example of a hospital antibiogram

8 The role of the infectious diseases service

Authors: Celia Cooper and Margaret Duguid

8.1 Key points

- Infectious diseases physicians give legitimacy to antimicrobial stewardship programs and play an important role by collaborating with local specialists to ensure that the team's goals are understood and met.

- The infectious diseases service makes an important contribution to formulary decision making, antimicrobial restriction policies, and the establishment and operation of antimicrobial approval systems.

- The infectious diseases service has a critical role in improving overall antimicrobial use through providing expert advice on the appropriate use of antimicrobials, education of prescribers, and developing and implementing evidence-based guidelines for antimicrobial treatment and prophylaxis as part of the antimicrobial stewardship team.

8.2   Recommendations

!   8.2.1   The antimicrobial stewardship team includes an infectious diseases physician or clinical microbiologist (if available).

8.2.2   Hospitals have access to an infectious diseases service that provides expert advice, educates prescribers, and plays a major role in the development and implementation of antimicrobial policy and prescribing guidelines.

8.2.3   Hospitals without an on-site clinical microbiologist or infectious diseases physician negotiate external support for antimicrobial stewardship activities.

8.3   Infectious diseases services and antimicrobial stewardship

Antimicrobial stewardship (AMS) includes limiting the use of inappropriate agents, and encouraging the appropriate selection, dosing and duration of antimicrobial therapy.[119] Infectious diseases (ID) specialists have played a major role in antimicrobial management for many years.[120] There is good evidence that their involvement improves antimicrobial use and clinical outcomes as well as reduces costs of antimicrobial therapy.[29, 120-121] ID services are considered essential to the success of AMS programs.[1, 12, 17-18] The success of many of the strategies to improve antimicrobial prescribing discussed in Part 1 are dependent on the involvement of the ID service. ID physicians lend legitimacy to AMS programs and can collaborate with local specialists to ensure that the AMS team's goals are understood and met.[12] Prescribing physicians need to have confidence in the person determining the appropriateness of antimicrobial requests. Clinicians caring for critically ill patients are considered more likely to be willing to follow an antimicrobial policy supported by their ID colleagues.[29]

The contribution of ID services to organisational AMS activities may include:

- leading the AMS program

- providing expert advice

- participating in

    » drug and therapeutics committees, and contributing to decision making for inclusion of all antimicrobials in their institution's formulary

    » prescribing review, intervention and feedback activities

    » the development, review and audit of clinical pathways and guidelines

    » the evaluation and reporting of hospital antimicrobial use

- establishing and maintaining antimicrobial approval systems in conjunction with the pharmacy department

- liaising with clinical departments and committees

- conducting antimicrobial education for medical staff, pharmacists and other clinical staff.

8.4 Leading the antimicrobial stewardship program

The presence of at least one ID physician with time to work on the development, implementation and function of the AMS program is considered essential to the success of the program.[1, 12] International guidelines recommend that an ID physician is a core member of the multidisciplinary AMS team[1, 12, 18] and the institution's AMS program should be led by an ID physician.[1, 12]

Gaining physician acceptance of antimicrobial interventions by ensuring there is no perceived loss of autonomy in clinical decision making is an important barrier that an ID physician can help overcome.[3]

Responsibilities for the lead ID physician in implementing an AMS program have been identified as:[17]

- establishing the AMS team

- integrating the functions of the AMS team with the drug and therapeutics, and infection prevention and control committees

- coordinating analysis and reporting of antimicrobial use

- ensuring availability of a process of feedback on antimicrobial prescribing to the prescribers and the AMS team

- identifying responsibility for

  » developing and instituting prescribing policies (including antimicrobial formulary and restrictions), guidelines and clinical pathways

  » reporting antimicrobial use

  » resourcing the above activities

- reporting to the hospital executive.

Obtaining the support of hospital administrators for the AMS program is essential to the effectiveness of the program. The lead ID physician, along with the director of pharmacy, should be given the authority and resources, including dedicated ID physician time, required to implement and maintain the AMS program and to monitor the outcomes of the program.[1, 12, 15]

Teaching hospitals should have at least one ID physician (or clinical microbiologist) on-site to participate in AMS activities. Smaller metropolitan hospitals, and rural and regional hospitals should consider employing part-time ID specialists or obtaining consultancy services from a hospital with an established ID service.

Smaller hospitals employing a part-time ID specialist can show improved antimicrobial use and significant antimicrobial cost savings.[1] LaRocco reported an antimicrobial team led by an ID physician (8–12 hours per week) and a clinical pharmacist performing review and feedback in a 120-bed, nonteaching community hospital three days a week effected a 19% reduction in antimicrobial costs.[41]

8.5 Consultation with infectious diseases services

Inadequate antimicrobial therapy and delays in treatment are associated with increased morbidity and mortality.[3,32] Inadequate antimicrobial therapy is an independent risk factor for death among critically ill patients with severe infection.[122] Studies have demonstrated an approximate 10% decrease in the mortality rate in patients with severe sepsis receiving adequate antimicrobial treatment when compared with those receiving inadequate therapy.[33]

Kollef cites consultation with an ID specialist as one of six clinical strategies to reduce inadequate antimicrobial treatment in the hospital setting.[32] There are numerous studies that demonstrate improved patient outcomes when ID physicians are consulted. Petrak et al. cite six studies where consultation by an ID physician for patients with bacteraemia reduced morbidity and mortality as well as the cost of care.[120] Byl et al.[123] evaluated 428 episodes of bacteraemia in a teaching hospital. Empirical treatment was appropriate for 78% of the episodes of bacteraemia treated by ID physicians compared with 54% when treated by other physicians ($P < 0.001$). Inappropriate empirical therapy was associated with a higher mortality rate. Similarly, in a retrospective review of management of *Staphylococcus aureus* bacteraemia, Filice and Abraham[124] demonstrated improvement in several areas when ID physicians were involved:

- Concordance with accepted standards for treatment was improved in cases where ID physicians were involved (97% versus 53%; $P = 0.0003$, Fisher exact test).

- Relapse was more likely in patients without ID physician involvement (29% versus 8%; $P = 0.02$, Chi-square).

- Infection cure and patient survival were higher when ID physicians were involved (85% versus 59%).

The study concluded that outcomes will be substantially better if ID physician involvement is provided for all cases of *S. aureus* bacteraemia.[124] Including an ID physician to evaluate patients' antimicrobial treatment as part of an enhanced infection control strategy has also been shown to contribute to significantly reducing the occurrence of vancomycin-resistant enterococcal infections.[125]

Early involvement of the ID service can improve the antimicrobial management of patients, ensuring appropriate dosage, duration and assessment of response. This can be achieved by including a range of infections within the hospital antimicrobial policy where early consultation with the ID service is advised. An example list from Hunter New England Health (Dr John Ferguson, Director of Infection Prevention and Control, Hunter New England Health, pers comm, October 2009) includes:

- infective spinal discitis or osteomyelitis

- infected joint replacements (early or late)

- bacterial meningitis (suspected or proven)

- bacterial or culture-negative endocarditis

- *S. aureus* bloodstream infection

- fever of unknown origin or where response to antimicrobial treatment is poor.

8.6 Antimicrobial formularies and approval systems

As discussed in Chapter 2, formulary restriction and prior approval is considered an essential component of any hospital antimicrobial management program. On average, these restrictive interventions have more than a three-fold effect on influencing proper prescribing when compared to persuasive interventions, such as education.[22] Fishman[14] cites prior approval as probably the single most effective intervention to improve antimicrobial use. The ID service has an important role to play in managing the approval process and developing a restricted formulary.

8.6.1 Formularies

ID staff should participate in the development and maintenance of the antimicrobial section of the hospital formulary, and the list of restricted antimicrobials. It is important that formulary decisions are informed by local microbiological information. The ID service should participate in the hospital's drug and therapeutics committee procedures involving antimicrobials, including:

- evaluating requests for new antimicrobials

- extending indications for existing products

- recommending products that should be restricted

- defining the criteria for prescribing restricted products.

This can be achieved through direct membership of the drug and therapeutics committee, or liaison between the committee and the ID service or AMS team. The ID service should also participate in a regular review of the antimicrobial formulary using facility-specific antimicrobial susceptibility data to guide decisions.

8.6.2   Approval systems

To be effective, antimicrobial approval systems require close collaboration between the ID (or clinical microbiology) and pharmacy services.

In 2004, ID physicians were surveyed in the United States, and most agreed that ID consultants should be directly involved in the approval process.[121] However, significant barriers have been identified, including the time involved in the authorisation process. To overcome this barrier, electronic approval systems may be used, or the approval process may be delegated to ID fellows or clinical pharmacists (with referral to an ID physician for expert advice).[12, 65, 126] Mechanisms for administering approval systems are discussed in Chapter 2.

Requests for antimicrobials provides an opportunity to educate prescribers.[121] If a conversation with the requesting doctor and an ID physician is required, opportunities are created to provide management advice as well as guidance on antimicrobial use.[127] Medical staff in an Australian teaching hospital reported finding the advice provided by an approval system managed by the ID unit to be useful and educational.[127] Sunenshine et al. reported similar findings in their survey of ID physicians in the United States.[121] Most prescribers in the Australian study believed the advice improved patient outcomes.[127] There have been concerns that a web-based antimicrobial approval program would reduce personal communication and education opportunities, but these systems actually facilitate communication and education while saving ID physician time.[65, 126]

8.7   Review and feedback strategies

The evidence for the use of antimicrobial review with intervention and feedback is discussed in detail in Chapter 3. Effective programs involve a member of the AMS team (an ID fellow or physician, or a clinical pharmacist) who reviews:

- orders for target drugs such as broad-spectrum antimicrobials
- potentially inappropriate antimicrobial therapy
- antimicrobial agents not concordant with hospital guidelines.[12]

An ID physician may be consulted if a conflict arises.

Review and feedback strategies are considered particularly important in streamlining antimicrobial use[12] and the ID service delivers the point-of-care interventions described in Chapter 4.

8.7.1   Antimicrobial stewardship team rounds

Antimicrobial stewardship team rounds provide the opportunity for ID physicians to discuss therapeutic options at the bedside with the treating clinician.[81, 106]

Intensive care units (ICUs), dialysis units, and oncology and bone marrow transplant wards are some of the primary areas associated with inadequate antimicrobial treatment[32] and could be the focus for AMS team rounds. At a minimum, ICU

patients should have their therapy reviewed by the AMS team. Patients can also be referred for review by the team by clinical pharmacists.

Inadequate treatment of bloodstream infections and nosocomial pneumonia, particularly in ICUs, are recognised as potential causes of increased patient morbidity.[32] All ICUs should have ID or clinical microbiology input. At rural hospitals, intensive care rounds can take place via teleconference with the on-duty intensivist in attendance. A pharmacist can assist in these rounds by assembling a list of the antimicrobials, dose and start dates for each patient prior to the round. The Healthcare Infection Control Special Interest Group provides guidelines for recommended ICU round processes.[a]

8.8 Antimicrobial policies, guidelines and clinical pathways

The ID service has an important role in the development, implementation, review and audit of antimicrobial policies, prescribing guidelines, clinical pathways and bundles of care. This supervision is considered necessary to ensure that prescribing guidelines, restriction policies and other activities are based on best evidence and that patients are not placed at risk.[12]

Several studies have demonstrated that clinical pathways and guidelines can be effective in improving patient outcomes and cost-effectiveness of treatment.[1, 128-129] Implementation of a multidisciplinary practice guideline in a surgical ICU led to a 77% reduction in antimicrobial use and cost, a 30% reduction in overall cost of care, decreased mortality and a trend to shorter hospital stay.[128] Martinez et al. found that the implementation of guidelines on patients with pneumonia was accompanied by an increase in the percentage receiving the process of care and a lower inpatient hospital mortality rate during the first 48 hours of care and after 30 days.[129] Clinical stability is also reached earlier in patients hospitalised for community acquired pneumonia when the antimicrobial treatment is begun early and complies with the recommendations.[129]

The long-term effect of guidelines on antimicrobial resistance remains to be determined. However, several studies on hospital acquired pneumonia and ventilator-associated pneumonia indicate that improving antimicrobial prescribing through use of guidelines may decrease emergence of resistant pathogens.[1]

8.8.1 Guideline and clinical pathway development

It is recommended that hospitals develop antimicrobial guidelines for treatment and prophylaxis for common infections relevant to the:

- patient population
- local antimicrobial resistance profile
- surgical procedures performed in the institution.

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a   www.asid.net.au/hicsigwiki

The *Therapeutic Guidelines: Antibiotic*[19] are recognised as a national standard for antimicrobial prescribing in Australia. Institutional clinical guidelines developed for local use should accord with these guidelines. They should incorporate local microbiology and resistance patterns and specify recommended agents(s), dose, route and duration of antimicrobial treatment for major categories of infection.[1, 15, 18]

The ID services should establish whether there are local reasons for varying from the national guidelines. The AMS team should be responsible for developing and regularly updating institutional antimicrobial prescribing guidelines in consultation with key clinicians or clinical opinion leaders.[3] Recommendations should refer to infections that occur with particular frequency in hospitals.[20] The United Kingdom Specialist Advisory Committee on Antimicrobial Resistance has published a list of common clinical syndromes appropriate for local antimicrobial treatment guidelines.[36] (See Section 1.11.1.)

Suggestions for prescribing guidelines that should be easily accessible to staff members are provided in Section 1.11.1. Some examples of guidelines are provided in Appendix 2, Section A.2.1.

8.8.2   Surgical prophylaxis

Surgical site infection is one of the most common healthcare associated infections.[2, 130] Prophylactic antimicrobial use has an important part to play in the prevention of postoperative wound and deep-site infections.[18] As much as one-third to one-half of antimicrobial use in hospitals is for surgical prophylaxis. Studies report levels of inappropriate use ranging from 30% to 90%, especially with respect to timing and duration.[19]

It is recommended that every surgical department should develop a guide for surgical prophylaxis appropriate for the type of surgery performed by staff in the department[20] (see the example in Appendix 2, Section A.2.1). The development and implementation of these guidelines should involve key players in surgical disciplines as well as the ID services. They should incorporate local microbiology and resistance patterns, and the selection pressure of antimicrobial use.[19-20] Third-generation cephalosporins (e.g. cefotaxime and ceftriaxone) should be avoided.[19]

Surgical prophylaxis guidelines should include: [19, 20, 130]

• the indication for prophylaxis (type of surgery)

• recommended antimicrobial, dose and route

Multidisciplinary development of evidence based practice guidelines incorporating local microbiology and resistance patterns can improve antimicrobial utilization.[1]

Treatment Guidelines … should be readily accessible, drawn up with multidisciplinary prescriber involvement, subject to peer review, evidence based where possible and compatible with national guidelines.[16]

- the preferred option being a single dose[a]

- instances where a second dose may be required (e.g. when procedures are delayed or prolonged (> 4 hours), or major intraoperative blood loss)

- an alternative agent where a beta-lactam antimicrobial is recommended as first line (for patients with a history of allergy to penicillins and cephalosporins)

- optimal time for administration (up to 60 minutes before induction).

8.8.3   Guideline implementation

Numerous studies have shown poor uptake of guideline recommendations.[107] Guidelines need implementation plans that are well developed, executed, sustained and embedded in comprehensive programs for change.[107] In a survey of New South Wales hospitals, 79% of respondents reported using the *Therapeutic Guidelines: Antibiotic*[19] as a basis of antimicrobial prescribing recommendations.[76] However, interventions to implement the guidelines were varied and inconsistent, and evaluation of the effectiveness of the interventions was not common practice.[76] The literature defines several barriers to proper guideline use by prescribers, including:

- feelings of lack of ownership

- loss of flexibility and professional autonomy

- beliefs that following guidelines can be burdensome and irrelevant to patient care

- lack of knowledge of existing physician practices.

These barriers need to be recognised and addressed as part of the local implementation plan for introducing prescribing guidelines.[76] Another significant barrier is that strategies for implementation at the local level are often not a part of national guidelines.[1]

ID staff should take an active role in implementing and evaluating antimicrobial policy and guidelines. Successful guideline implementation requires the support of motivated individuals to facilitate change[131] and research has shown that clinicians are more likely to follow a policy that is supported by their ID colleagues.[29, 127]

There is good evidence that guideline implementation can be facilitated through education and feedback on antimicrobial use and patient outcomes.[1] Compliance is also improved by promoting the ownership of guidelines through the development of local guidelines, or adapting the national guidelines to suit the local circumstances.[12] A study in the Netherlands reported increased compliance (from 67% to 86%) after revised guidelines were introduced, when physicians were widely consulted in the revision of guidelines for antimicrobial therapy, followed by active dissemination.[132]

In teaching hospitals, where senior medical clinicians influence trainees' prescribing, it is particularly important that senior staff engage in the implementation process

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a There is consistent evidence that a single dose of an antimicrobial agent with a half-life long enough to achieve activity throughout the operation is adequate for many types of commonly performed surgery.[130]

through involvement in local guideline development. Aiming education at authoritative senior department staff has been shown to have a significant impact in changing surgical antimicrobial prophylaxis practices.[12]

One barrier to appropriate prescribing is that senior clinicians and registrars are not aware of local and national resources that are available to support decision making.[99] The ID service and AMS team can promote the existence of antimicrobial prescribing guidelines, educate staff and liaise with hospital management to ensure the guidelines are readily available at the point of care. This can be achieved by making the guidelines available through several sources, including pocket-sized printed editions, the institution's intranet and other technology such as personal digital assistants.[3] Embedding guidelines into clinical decision support for electronic prescribing systems will provide further opportunity to guide prescribing at the point of care.

8.8.4   Maintenance of guidelines and clinical pathways

Guidelines and clinical pathways need to be regularly reviewed by the AMS team — a minimum of annually has been recommended.[17] They need to consider the latest version of the *Therapeutic Guidelines: Antibiotic*,[19] and local microbiology and resistance patterns, which require the input of ID staff.

An important part of this process is ensuring that only the latest versions of clinical guidelines and pathways are available for use.

8.8.5   Evaluating interventions and monitoring antimicrobial use

Evaluation of the use of prescribing guidelines and providing feedback to prescribers is an important step in the quality-improvement cycle, as well as a useful strategy to promote the use of guidelines and clinical pathways, and influence prescribing (see Chapter 3).[1, 17-18] Auditing an organisations' antimicrobial use also identifies whether implementation strategies are effective and whether different approaches are needed. Monitoring the use of guidelines and their outcomes, including the use of quality use of medicines indicators for antimicrobial therapy, is discussed in more detail in Chapter 5.

Continuous surveillance of antimicrobial use is considered an essential component of AMS programs. ID services should contribute to establishing and evaluating an antimicrobial surveillance system in their organisation. The data produced can be used to assess the need for programs to reduce antimicrobial use, and to scope programs and evaluate whether they are effective. Measuring the rate of antimicrobial use in adult patients by using a ratio of defined daily dose per occupied bed-days is recommended. (See Appendix 1.)

ID staff should also coordinate participation of the hospital in state or national antimicrobial surveillance systems, and advise on the local use of the data (refer to Appendix 1 for details on the National Antimicrobial Utilisation Surveillance Program and reporting measures).

ID staff should:

- advise the AMS team on areas to target for review or on antimicrobial usage evaluation studies

- assist in results analysis

- help to produce reports and recommendations for the committees of

  » drug and therapeutics

  » infection control and prevention

  » health service safety and quality.

See Chapter 5 for detailed discussion on monitoring antimicrobial use.

8.9 Liaising with other clinical departments and committees

Effective AMS programs require collaboration between the ID services and other departments and committees, including:

- clinical departments — with the development and implementation of policies and guidelines, and providing education and feedback on results of audits and drug usage evaluation studies

- pharmacy staff — with restricted formulary and approval system management, and the provision of expert advice and support for other AMS interventions described in Part 1; this may include consultation when a conflict arises[12]

- infection prevention and control staff — it is recommended that an ID physician takes a leadership role in the management of the hospital's infection control and prevention program. This provides the ideal opportunity for infection control practices to be enhanced by AMS activities in the control of outbreaks of resistant organisms.

8.9.1 Infection control professionals

Infection control professionals (ICPs) can play an important role in AMS activities and should be included in the hospital's AMS team.[1] Integrating the AMS program with the hospital's infection prevention and control progam provides opportunities to synergistically reduce antimicrobial resistance and improve patient outcomes.[12] Data collected by ICPs on nosocomial infections may be useful to evaluate the outcomes of AMS activities.[12] ICPs can include information on AMS in their infection control education programs for healthcare workers — including nursing staff responsible for administering antimicrobials and collecting microbiology specimens. Integrating principles of AMS into infection control education can contribute to the hospital's efforts in preventing emergence of antimicrobial

resistance and subsequent transmission. This education can also cover the correct collection, handling and transport of specimens to avoid degradation or contamination of specimens. ICPs aware of their organisation's antibiogram can be alert to trends in local resistance patterns and the need to instigate increased infection prevention measures in patients colonised or infected with multiresistant organisms.

8.10 Education of staff

One of the primary roles of the ID specialist is that of a teacher.[120] Education can be provided as part of a multidisciplinary program,[17] with presentations at grand rounds or as part of an intervention (e.g. during the approval process or feedback following review of antimicrobial prescribing). Petrak et al. describe '… an ID consultation that is written, verbally discussed, supported by literature, and refocused as the case evolves' as the perfect model for educating healthcare staff.[120]

Using education as a strategy to influence prescribing behaviour is discussed in detail in Chapter 6.

8.11 Interactions with pharmaceutical companies and their representatives

The influence of the pharmaceutical industry on the prescribing of medicines is discussed in detail in Chapter 6. Studies of interactions between medical professionals and the pharmaceutical industry[110-112] confirm that these interactions can increase formulary-addition requests (even when there was no therapeutic advantage over existing formulary drugs) and affect prescribing practices. These findings highlight the importance of educating prescribers about the influence of pharmaceutical industry relationships and sponsorship on prescribing behaviour.

The ID service should not only be involved in the provision of this education at undergraduate and postgraduate levels, but the ID physicians themselves need to exercise caution in their interactions with pharmaceutical companies and their representatives. They should actively support the development and implementation of hospital policies that restrict staff access to pharmaceutical representatives, and support the adoption of conflict of interest guidelines developed by professional societies or colleges (see Appendix 2, Section A2.2 for a list of available Australian guidelines and policies). These guidelines should be incorporated into hospital policy and training programs. This topic is further discussed in Chapter 6.

9 The role of the pharmacy service

Authors: Margaret Duguid and David Kong

9.1 Key points

- Pharmacists are essential to the success of antimicrobial stewardship programs and have a positive effect on improving appropriate antimicrobial use, patient care and safety.

- Hospital pharmacists are well placed to prospectively or retrospectively review antimicrobial orders, provide feedback to prescribers, and identify cases requiring review and referral to the nominated antimicrobial stewardship health professional or team.

- A pharmacist with experience and training in antimicrobial stewardship is a key member of the antimicrobial stewardship team. Their prime role is to champion and coordinate the activities of the hospital's antimicrobial stewardship program in collaboration with the antimicrobial stewardship program leader.

- The responsibilities of pharmacists in antimicrobial stewardship include:

  » providing expert advice and education to relevant hospital staff

  » contributing to ward rounds, consultations and relevant hospital committees (e.g. antimicrobial stewardship committee or drug and therapeutics committee)

  » participating in policy development and the application and maintenance of antimicrobial formulary and prescribing guidelines

> » implementing and auditing activities that promote safe and appropriate use of antimicrobials

> » being involved in research activities related to antimicrobial stewardship.

9.2 Recommendations

! 9.2.1 The antimicrobial stewardship team includes a pharmacist who has experience or is trained in antimicrobial stewardship, and who is allocated time and resources for antimicrobial stewardship activities.

9.2.2 Pharmacists review antimicrobial orders for adherence to local guidelines and provide timely feedback (where applicable) to the prescriber.

9.2.3 Pharmacists are supported by the hospital in enforcing antimicrobial prescribing policies, including formulary restrictions and encouraging adherence to local prescribing guidelines.

9.2.4 Hospitals support training for pharmacists to equip them with the knowledge and skills required to effectively participate in antimicrobial stewardship activities.

9.4.5 Mechanisms are in place to allow pharmacists to seek expert advice from, and refer to, a clinical microbiologist or infectious diseases physician.

9.3 Pharmacy services and antimicrobial stewardship

Pharmacists are key to the success of antimicrobial stewardship (AMS) programs in hospitals and play a number of roles in assisting with strategy implementation that encourages responsible use of antimicrobials.[1, 12, 85, 133] A Cochrane review of interventions to improve antimicrobial prescribing identified 66 studies with interpretable data. In 22 of these studies, pharmacists delivered persuasive (64%), restrictive (23%) and mixed (14%) interventions aimed at reducing prescribing of antimicrobials.[34]

Although the main focus of this section is the role of the infectious diseases (ID) pharmacist in AMS, it is important to acknowledge that pharmacy administrators, clinical pharmacists and those involved with the supply of antimicrobials all make an important contribution to developing and maintaining AMS programs in hospitals.

9.4 Pharmacy administration

The AMS team requires the support of hospital administrators.[1] The director of pharmacy has an important role in establishing communication and collaboration between the staff from pharmacy, microbiology or IDs, and infection prevention and control. The director of pharmacy is also responsible for maintaining the formulary management system, and supporting the activities of the drug and therapeutics committee in evaluating antimicrobials for listing on the hospital's formulary and in monitoring antimicrobial use.

9.5 Pharmacists providing clinical and dispensary services

The review of antimicrobial prescribing with prescriber feedback has been identified as a key strategy in achieving prudent use of antimicrobials (see Chapter 3). Hospital pharmacists are well placed to identify antimicrobial use requiring review and can refer cases to the nominated AMS health professional or team.[12]

Dispensary and clinical pharmacists play an important part in supporting AMS strategies by ensuring formulary restrictions and practice guidelines are followed, and by participating in activities that promote safe and prudent use of antimicrobials. Studies have shown that pharmacists' interventions have a positive impact on the effective and appropriate use of antimicrobials.[134] Clinical pharmacists, with the support of the AMS team, need to be empowered to provide prescribing information and feedback to prescribers.[17]

9.6 Specialist infectious diseases pharmacists

A clinical pharmacist with ID training is considered a core member of the multidisciplinary AMS team.[1] The ID pharmacist's role may include a clinical service to a ward or medical unit with high antimicrobial consumption, such as intensive care or surgical units.[102] Alternatively, the ID functions may be included within the role of the pharmacist responsible for drug usage evaluation (DUE) or quality use of medicines. Whatever the position, the pharmacist should be allocated the time and resources to undertake AMS activities.[1] In the United Kingdom, the employment of specialist antimicrobial pharmacists facilitated greater interaction between the pharmacy and microbiology or ID departments, and demonstrated significant reductions in antimicrobial acquisition costs.[135]

At this time in Australia there are few pharmacists with specialist ID training. For the purposes of this chapter the term ID pharmacist encompasses those pharmacists with experience or training in antimicrobial stewardship who have responsibility for AMS activities.

9.7 Roles and responsibilities of infectious diseases pharmacists

The skills and responsibilities of an ID pharmacist is supported by current literature and are discussed in the following sections. They serve as a basis for deriving a job description for an ID pharmacist.

9.7.1 Prime role

The prime role of an ID pharmacist is to coordinate the activities of the hospital's AMS program in collaboration with the AMS program leader. Their aims are to achieve cost-effective, quality use of antimicrobials and reduce the emergence of antimicrobial resistance.

9.7.2 Responsibilities

The responsibilities of an ID pharmacist may include:

- providing expert advice

- attending ward rounds

- liaising with other departments

- antimicrobial formulary management

- developing and maintaining antimicrobial guidelines

- point-of-care interventions

- monitoring antimicrobial use

- educating medical and nursing staff, students and others

- demonstrating leadership in AMS

- carrying out research.

The infectious diseases physician and head of pharmacy should negotiate with hospital administration to obtain adequate authority, compensation, and expected outcomes of the program.[1]

9.7.3 Expert advice

ID pharmacists can advise other pharmacists and prescribers on the management of antimicrobial therapy in individual patients. They can act as a triage for cases requiring input by microbiology and ID clinicians.[135] This may include the choice, dose and duration of antimicrobial therapy.[1, 34] The optimisation of dosage — based on individual patient characteristics, causative organisms, the site of infection, and pharmacokinetic and pharmacodynamic characteristics of the drug — has been cited as an important part of AMS (see Chapter 4 for further details).[1] Prospective review of antimicrobial orders and timely follow up with the prescriber by an ID pharmacist reduces inappropriate use of antimicrobials and leads to improved clinical outcomes.[1, 12]

Providing expert advice includes informing senior hospital management and relevant medical units on the AMS program and activities within the hospital.

9.7.4 Antimicrobial stewardship ward rounds

ID pharmacists should attend joint ward rounds with microbiology and ID clinicians to review patients with complex antimicrobial management problems and those who have been referred to the AMS team. These rounds may include regular rounds in units with complex antimicrobial management issues such as intensive care or haematology units.[135]

9.7.5 Liaison

Liaising (on behalf of the pharmacy department) with other departments and committees is an important role for ID pharmacists (Table 9.1).

Table 9.1 Pharmacy liaison with departments and committees

Department or committee	Liaison activity
Microbiology, ID and other departments	• antimicrobial formulary • introduction of new antimicrobials • unexpected changes in antimicrobial use patterns • the development of policies related to AMS activities within the hospital[102]
Microbiology and ID staff	• changes in antimicrobial sensitivities • updating the hospital formulary information and guidelines accordingly

Hospital committees and management	• matters related to AMS
	• active participation in relevant hospital committees such as:
	  » the AMS committee or antimicrobial subcommittee of the drug and therapeutics committee;[102] the ID pharmacist may provide the secretarial support to this committee
	  » the infection prevention and control committee[102]

Professional organisations, for example: • Society of Hospital Pharmacists of Australia Infectious Diseases Committee of Specialty Practice * • Healthcare Infection Control Special Interest Group+	• matters related to AMS

AMS = antimicrobial stewardship; ID = infectious diseases
* www.shpa.org.au/scripts/cgiip.exe/WService=SHPA/ccms.r?PageId=7
+ www.asid.net.au/hicsigwiki

9.7.6 Antimicrobial formularies and approval systems

Restricted formularies and antimicrobial approval systems are effective in improving antimicrobial use in the hospital setting (see Chapter 2). ID pharmacists have an important role in supporting and maintaining hospital prescribing control systems by:

• participating in the antimicrobial formulary management process, including reviewing the evidence for inclusion of new antimicrobials or deletion of existing agents from the formulary for consideration by the drug and therapeutics committee

• updating the hospital's formulary and antimicrobial prescribing guidelines in accordance with the drug and therapeutics committee decisions — including updating information and alerts within clinical decision-support systems for electronic prescribing, dispensing and antimicrobial approval systems (see Chapters 2 and 10)

- educating and supporting other pharmacists in the clinical and dispensary areas to enforce antimicrobial prescribing programs and policies, and encourage compliance with prescribing guidelines[34] — this may include providing advice (with support from the AMS team) in those situations where there is debate with clinicians who wish to prescribe outside the hospital's policy[102]

- monitoring compliance with the hospital's antimicrobial prescribing policies, and liaising with microbiology and ID clinicians regarding issues of noncompliance.

9.7.7 Antimicrobial guidelines

ID pharmacists should work with microbiology, ID and other relevant clinicians to develop and maintain:

- antimicrobial prescribing guidelines, including specific unit protocols; for example, guidelines for antimicrobials in the management of febrile neutropenia

- policies for antimicrobial serum-level monitoring, such as aminoglycosides and glycopeptides, and for training clinicians and pharmacists about safe and effective dosing practices.[135]

This responsibility includes ensuring that the latest versions of prescribing guidelines are available in hard or soft copy from the hospital (such as printed pocked-sized versions and electronic versions on the intranet). The electronic version can be incorporated into the appropriate clinical decision-support systems within electronic prescribing, dispensing and administration systems.

9.7.8 Point-of-care interventions

ID pharmacists can play a leading role in implementing policies and interventions that promote safe and appropriate use of antimicrobials. These activities are discussed in more detail in Chapters 1 and 4 and include:

- intravenous-to-oral switch programs[1, 135]

- antimicrobial stop orders[102]

- therapeutic substitution of antimicrobials[102]

- systems for obtaining and recording approvals for restricted antimicrobials, such as mandatory order forms, telephone or online approval systems[1, 136]

- streamlining therapy to narrow-spectrum agents when culture and sensitivity results are available[1, 102]

- developing and disseminating clinical decision tools such as antimicrobial dosing cards for common infections.

9.7.9   Audit and evaluation of antimicrobial use

ID pharmacists should generate and collate reports on antimicrobial use for the AMS team, the drug and therapeutics committee, infection control committee and heads of clinical units. The reports may include:

- regular (monthly) reports from pharmacy records of antimicrobial use and expenditure at hospital or clinical unit level (i.e. total antimicrobial use, restricted antimicrobials or specific antimicrobial groups)

- national comparative data in terms of defined daily doses per 1000 occupied bed-days for those hospitals submitting to the National Antimicrobial Utilisation Surveillance Program.

ID pharmacists may also conduct DUE activities. These may be:

- point prevalence studies to identify the percentage of patients prescribed antimicrobials, the number of anti-infectives per patient, the indication for use and the duration of therapy

- clinical audits of a specific antimicrobial or group of antimicrobials against local guidelines (e.g. indications for prescribing, sensitivity to the antimicrobial, empirical versus treatment, doses prescribed and duration of therapy)

- local or collaborative DUE projects such as those organised by the National Prescribing Service, including implementation and evaluation of interventions to influence prescribing behaviour.[137]

Process and outcome measures have been shown to be useful in determining the impact of AMS on antimicrobial use and resistance patterns.[1] ID pharmacists are well placed to coordinate feedback from stakeholders with respect to the success of AMS activities and the collection of data for monitoring indicators to measure performance in safe and effective antimicrobial use. This includes indicators for antimicrobial therapy in the *Indicators for Quality Use of Medicines in Australian Hospitals*.[95] See Chapter 5 for further discussion on quality improvement activities and monitoring antimicrobial use.

9.7.10 Education

Chapter 6 discusses the importance of prescriber education and the content of training programs.

ID pharmacists can play an important role in educating staff about AMS. This may involve:

- educating pharmacy, medical, and nursing staff and students on principles of judicious, safe and effective antimicrobial prescribing, and the concept of resistance[135]

- informing prescribers on antimicrobial prescribing guidelines and policies, including educating junior doctors during their initial orientation and reinforcing information

at roster changes, and presenting results of clinical audits and DUE studies in forums such as medical teaching rounds[135]

- employing active educational techniques such as academic detailing, using one-on-one education sessions with clinicians — this has been shown to improve prescribing behaviour more than passive dissemination of information (such as supplying posters or printed handouts).[12, 34]

9.7.11 Leadership in antimicrobial stewardship

ID pharmacists should play a leadership role within the AMS program, advocating the implementation of activities within the hospital that aim to improve prescribing and the quality use of antimicrobials. They should also support pharmacy staff and others (especially junior staff) on issues related to the AMS program within the hospital (e.g. resolve disagreements about antimicrobial prescribing practices).[17, 135]

9.7.12 Research and development

ID pharmacists should (where possible) be actively involved in coordinating and participating in research and practice development activities related to AMS.[135] This is especially important for pharmacy-led interventions in AMS. Pharmacists should publish results in peer-reviewed publications and present data at conferences.[135]

9.8 Skills and training

ID pharmacists should be experienced clinical pharmacists with expertise in antimicrobials and the pharmaceutical management of infectious diseases.[102, 135] Postgraduate training in ID and the ability to interact with senior clinicians on a credible level are considered highly desirable attributes.[3, 102]

There is a shortage of pharmacists with ID training and this has been identified as one of the barriers to implementing hospital AMS programs.[23] Currently, there are no training courses in Australia for pharmacists to attain the skills and knowledge required to coordinate an AMS program. In the United States, professional pharmacy organisations have been asked to consider developing a pharmacist-focused AMS curriculum.[23] Such a curriculum would encompass important concepts in antimicrobial therapy, the use of guidelines and other literature supporting AMS, and the practicalities of establishing and maintaining an AMS program.[23] Developing a similar curriculum for Australia, or including pharmacists' education in training resources developed for prescribers, would assist in building the capacity of pharmacists with the skills required to effectively participate in AMS programs (see Chapter 6).

Properly trained clinical pharmacists acting in concert with physician colleagues have been shown to make a substantial impact on patient care in a variety of practice settings including infectious diseases.[12]

10 Use of computer technology to support antimicrobial stewardship

Author: Karin Thursky

10.1 Key points

- Electronic clinical decision-support systems are potentially useful tools in antimicrobial stewardship programs.

- Organisational, social and cultural issues relating to prescribing behaviour are the key factors that determine the effectiveness of these systems, and resources should be directed towards addressing these issues during implementation.

- Electronic decision support must be integrated into the clinical workflow to be effective in a complex clinical domain such as antimicrobial prescribing.

- Electronic stewardship systems are most likely to be successful as part of a multidisciplinary antimicrobial stewardship program.

10.2 Recommendations

10.2.1 Hospitals work towards implementing electronic decision-support systems to guide antimicrobial prescribing and integrating these systems with electronic health records, and electronic prescribing and medication management systems.

10.2.2 An antimicrobial stewardship pharmacist and antimicrobial stewardship team are available to support and maintain electronic stewardship systems.

10.2.3 Antimicrobial stewardship teams have access to patient administrative data, microbiology data (including antimicrobial resistance) and drug use data for monitoring and reporting purposes.

10.3 Use of computer technology to support antimicrobial stewardship

The years 2010–20 will see the development of electronic medical records, electronic prescribing and computerised clinical decision support in hospitals. There is a move towards electronic medication management in the acute healthcare setting in Australia, with both state and federal government-sponsored initiatives to modernise the healthcare information technology infrastructure.[a] This will provide opportunities to integrate antimicrobial stewardship (AMS) activities with electronic prescribing and medication management systems.

Electronic clinical decision-support systems (CDSS) appear to improve the quality of prescribing and reduce the costs of antimicrobial prescribing, but their overall cost-effectiveness, and impact on patient outcome and antimicrobial resistance is much less certain. There have been two published reviews on CDSS and its use in antimicrobial prescribing.[138-139] Current opinion from key infectious diseases bodies supports the use of CDSS as potentially useful tools in AMS programs, and the use of electronic antimicrobial approval systems has been recommended by both the Victorian and New South Wales health departments.[140, b]

10.4 Electronic antimicrobial decision-support systems

Electronic CDSS can be as simple as online access to formulary restrictions, local antimicrobial prescribing guidelines and *Therapeutic Guidelines: Antibiotic*[19] via the hospital intranet. More complex systems can include integrated CDSS embedded within other applications, such as pharmacy dispensing systems or electronic prescribing systems.

10.4.1 Use and benefits of electronic decision support in antimicrobial stewardship

There have been several systematic reviews evaluating the effectiveness of CDSS and e-prescribing systems.[141-144] CDSS appears to be effective in reducing medication error, and increasing physician guideline uptake and concordance.[141-144] The most effective CDSS were those that were coupled to an electronic medical record or e-prescribing system. However, there are very few published examples of antimicrobial CDSS embedded in electronic prescribing systems and these are confined to two major institutions in the United States.[52, 63]

The Antibiotic Assistant program at the Latter Day Saints Hospital, Utah,[52] is an advanced CDSS able to generate patient and situation-specific antimicrobial treatment recommendations based on data from the individual electronic health record. The results of the antimicrobial management program were reported in 1998[52] and the study is widely cited in the literature as the benchmark for CDSS in antimicrobial control.[145] The before-and-after study was performed in the 12-bed

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a www.health.gov.au/internet/main/publishing.nsf/Content/National+Ehealth+Strategy

b www.health.nsw.gov.au/resources/quality/hai/pdf/mros_keyrecommendations.pdf

intensive care unit in 1992–95. There was a significant reduction in antimicrobial mismatches, drug alerts, adverse drug events (ADEs) and hospitalisation costs in those patients in whom the program was followed. This was in comparison with the historical cohort or in the patients in whom the program was overridden. Interestingly, only 46% of antimicrobial selection recommendations were followed, compared with 94% of antimicrobial dosing suggestions. Four years after this study was reported, a prospective study was performed to evaluate the concordance between physician's orders and the recommendations made by the program. Of the 1078 physicians' and Antibiotic Assistant order days, there was only 33% concordance. The authors attribute this fall in concordance to insufficient monitoring of clinician satisfaction or acceptance of information (or both), as well as insufficient education.[146]

Other antimicrobial decision-support systems can be classified as task-specific, such as those providing microbiology result-independent prescribing and those that provide microbiology result-guided prescribing.[138-139] They may be asynchronous (i.e. they do not provide decision support at the time of prescribing). These are specialised knowledge-based expert systems that issue clinical alerts that are communicated to the clinicians after the antimicrobial is ordered. These systems include pharmacy-based antimicrobial CDSS that monitor antimicrobial prescriptions in relation to microbiology reports and generate reports of potential therapeutic mismatch.[147-152] In all of these studies, full-time, dedicated, trained pharmacists were responsible for reporting the results to the treating clinicians. The majority of these systems reported reductions in antimicrobial expenditure and the use of targeted antimicrobials.

Benefits that can be achieved through effective communication between these systems are similar to those demonstrated with e-prescribing systems and include:

- appropriate antimicrobial choice (based on microbiology results)
- optimal antimicrobial dosing and monitoring (based on pathology results)
- improved clinician response time
- broader use in quality improvement activities (antimicrobial resistance and simultaneous microbiology surveillance).[153]

Even now, few hospitals have links between pharmacy and laboratory databases, because these systems are usually incompatible commercial systems. However, improved communication between the pharmacy and the laboratory can be achieved without specialised software.[154] An Australian study in an intensive care unit demonstrated that significant changes can be achieved in antimicrobial utilisation with improved display of microbiology results and point-of-care recommendations for positive isolates.[155] As more advanced hospital systems are introduced, these barriers will be fewer, although significant challenges remain in ensuring that clinical decision support is appropriate and integrated into workflow for AMS.

In Australia, improvements in prescribing practices have been demonstrated with the IDEA3s electronic antimicrobial advice and approval system,[65] and Guidance

DS, a transferable web-based AMS program developed by the Royal Melbourne Hospital.[66] Over the three years since deployment of Guidance DS, longitudinal time series analyses of antimicrobial use and the hospital antibiogram demonstrated significant improvements in the use of broad-spectrum antimicrobials and an associated reduction of resistance in some gram-negative bacteria.[66] The use of these products in AMS is described in Chapter 2.

10.4.2 Other uses of clinical decision-support systems in antimicrobial stewardship

There are several examples where CDSS have been developed to assist with the identification of patients at high risk for nosocomial infection using data from the electronic patient record, and microbiology, pathology and radiology results.[156-159] These systems can be used in early infection prevention programs and for surveillance activities.

10.5 Electronic prescribing and medication management systems

Electronic prescribing (e-prescribing) systems are computer applications that allow clinicians to generate paper or electronic medication prescriptions. Electronic medication management systems (eMMS) are information systems that manage each phase of the medication management process:

• decision support

• computerised physician order entry (e-prescribing)

• medication review

• dispensing

• recording medicines administration.

Although electronic systems for ordering medicines are well established in general practice, only a small number of sites in Australia have implemented inpatient e-prescribing. However, commercial e-prescribing and eMMS systems will be implemented across many institutions within the next 5–10 years. These commercial solutions will require substantial organisational changes and incur significant costs. The high cost of implementing e-prescribing systems, and the challenges of integrating into existing information systems and convincing physicians to use these programs, largely explains the low prevalence of these systems in both American and Australian hospitals.[1] According to the Leapfrog Group,[a] the costs of implementing e-prescribing systems will far exceed potential savings from drug-cost avoidance and ADE avoidance in most hospitals.[160] In Australia, the majority of hospitals lack the foundations required for successful implementation of eMMS. Many are in a state of transition between paper-based medical records and electronic medical records.

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a The Leapfrog Group supports improvements in the safety, quality and affordability of health care. It is an initiative of purchasers of health care in the United States: www.leapfroggroup.org.

Currently available commercial e-prescribing software systems have limited decision-support capability that is largely limited to rule-based decision support. The majority of antimicrobial decision support in commercial hospital eMMS is limited to commercial drug-interaction packages or drug-information databases. Almost all commercial systems are associated with front-end decision support provided at the time of prescribing such as default values, routes of administration, dose and frequencies. They may also include drug-allergy checks, drug interaction and drug-laboratory value checks. However, the use of front-end alerts can cause frustration for clinicians if numerous warnings pop up during order entry[161] and they may start overriding such alerts.

The safety of commercial e-prescribing systems providing decision support is largely unknown, and there are emerging reports of systematic medication errors occurring with some systems if not safely implemented.[162-163] Computerised ordering and prescription tools have been advertised as means to reduce the frequency of ADEs.[164-165] However, evidence exists that electronic systems cannot prevent all errors or ADEs and may, in some situations, be responsible for new types of errors. Examples include pharmacy inventory displays being mistaken for guidelines, or antimicrobial renewal notices being ignored when placed on the paper chart rather than on the electronic chart.[163] While e-prescribing systems eliminate the need for transcription and ensure legibility, inadequate decision support for drug selection and dosing will 'redistribute' error frequencies.

10.5.1 Integrating stewardship programs with electronic medication management systems

AMS can be integrated into eMMS decision support in several ways. Examples of using simple rule-based decision support to direct the selection of the appropriate antimicrobial and dosage regimen at the time of prescribing include:

- informing users of prescribing restrictions and the hospital-approval criteria
- assisting with dosing
- stop order reminders or flags
- order sets containing prophylaxis and treatment recommendations (e.g. an order set for treating community acquired pneumonia would list antimicrobials and dosage regimens approved by the hospital drug and therapeutics committee)[23]
- providing direct access to *Therapeutic Guidelines: Antibiotic*[19] and local hospital antimicrobial prescribing guidelines.

Commercial e-prescribing systems should support third-party applications that can provide advanced antimicrobial decision support at the point of care, or facilitate the stewardship process. Several examples of CDSS that are not integrated into an eMMS are described in Section 10.4 and the literature supports such task-specific decision support.

In addition to improving the quality of prescribing and reducing costs of antimicrobial use, eMMS can provide data on individual patient use of antimicrobials from the record of doses administered. This data can better inform drug use monitoring and quality improvement activities.

In the short term, many sites will introduce and use CDSS that do not rely on eMMS, although the ideal situation is that commercial eMMS would support third-party CDSS that are effective in the Australian healthcare sector.

10.6 Information technology requirements

One of the major barriers to the adoption of electronic processes for AMS has been a lack of information technology (IT) infrastructure or support in individual institutions. Decision-support systems have complex requirements, such as medical data dictionaries and coding systems that have, until recently, been lacking. As a result, many systems have been 'home grown', using databases developed by local content experts and IT solutions tailored to the institution. The transferability of these systems, and therefore the ability to generalise from the results, is limited. Newer concepts, such as the use of archetypes to attempt to capture complex meaning, will provide the information required for electronic health records and advanced decision support.[a]

IT requirements to support AMS can be considered at institutional, state and national levels. Data sharing between sites both at a state and national level will be essential for benchmarking. Minimum requirements for individual institutions, in order of importance, are:

- real-time integrated patient and institutional data

- access to local and reference guidelines

- access to culture and susceptibility results with an effective microbiology browser

- access to antimicrobial dispensing information from pharmacy systems so that dispensing data can be tracked

- access to hospital and unit-specific antibiograms

- availability of alerts (e.g. drug interactions, patient-specific risk factors).

Unique patient identifiers across area health networks will support the tracking of patients across institutions and data collection (this currently exists in Queensland, Tasmania, Western Australia and New South Wales).

Finally, business models for healthcare institutions planning to implement eMMS should support access to and use of data from commercial applications.

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a www.openehr.org/home.html

10.7 Implementing antimicrobial computerised decision-support systems

Antimicrobial CDSS should always be considered as only one part of an effective AMS program. The requirements for implementing antimicrobial CDSS are therefore similar to those required for AMS in general, and are discussed in Chapter 1 and Chapter 2, Section 2.5.5.

Implementation must be carefully planned if CDSS is to improve the safety and quality of prescribing. Organisational, social and cultural issues relating to doctor prescribing behaviour are the key factors that will determine the effectiveness of these systems. Resources should be directed towards understanding and addressing these issues when implementing CDSS in the healthcare sector (see Chapter 2, Section 2.5.5).[166] It has been estimated that the failure rate of new IT systems in health care is 25–50%.[167] Attention to the organisational and cultural changes that the systems bring is required for success, along with the integration of pharmacy and laboratory systems.

Organisational change theory provides important insights into the key factors that contribute to the successful deployment of a CDSS.[168-169] Using the example of an antimicrobial CDSS, there needs to be:

- a willingness to adopt a new system by the executive and clinicians

- sufficiently experienced personnel for project management; in the case of antimicrobial CDSS this is usually a senior pharmacist with experience in AMS

- an established AMS program as discussed in Chapter 1 and Chapter 2, Section 2.5.5

- a well-planned and well-timed publicity campaign using the intranet, grand rounds, unit meetings and posters

- administrative support, including financial support for the project team that will require dedicated time to carry out the implementation and deployment

- specific qualities of the CDSS, such as usability, functionality and integration into the clinical workflow.

After implementation, resources need to be available to develop and maintain the CDSS. This includes maintenance of the formulary, revision of guidelines and the use of order sets for antimicrobials that accord with the hospital formulary, prescribing guidelines and clinical pathways.

Antimicrobial CDSS are likely to remain a cost-effective alternative to e-prescribing systems, including those provided by pharmacy-based systems or web-based tools that are not necessarily integrated with e-prescribing systems. It is important for sites planning to implement eMMS to integrally involve AMS in the planning and roll-out of the system to ensure that quality and safety standards are maintained.

Appendixes

Appendix

1

Antimicrobial usage: monitoring and analysis

Chapter 15 from: *Reducing Harm to Patients from Health Care Associated Infection: the Role of Surveillance.* Eds Cruickshank M, Ferguson J. Australian Commission on Safety and Quality in Health Care, July 2008. The references for this chapter begin on page 139.

Authors: M Duguid, J Ferguson, V McNeil, I Wilkinson

Key points

- Monitoring and analysis of antimicrobial usage is critical to understanding antimicrobial resistance and to monitoring effects of containment strategies.

- Methods of antimicrobial data collection differ, but most institutions provide population surveillance data obtained from computerised pharmacy records.

- Surveillance data can be used to identify changes in usage that may be linked to development of resistance and to measure the impact of antimicrobial stewardship programs.

- Antimicrobial stewardship programs have been shown to reduce resistance rates, morbidity, mortality and cost.

- Comprehensive, integrated surveillance programs operate in the United States and Europe, where programs include the European Surveillance of Antimicrobial Consumption, the Danish Integrated Antimicrobial Resistance Monitoring and Research Program, a surveillance program for antimicrobial consumption and resistance in the Netherlands, and the Swedish *Antimicrobial Utilisation and Resistance in Human Medicine* report. In Europe, reports on antimicrobial consumption and resistance are published annually.

- In Australia, the National Antimicrobial Utilisation Surveillance Program provides monthly reports on hospital inpatient antimicrobial usage to contributing hospitals, and bi-monthly reports to the Australian Department of Health and Ageing. Data are contributed by 50% of principal referral hospitals from six states.

- Comparison with international data shows that Australian usage rates in hospitals are high for some antimicrobial classes. The total use of antimicrobials in the Australian community falls in the middle of the range recorded in European countries.

- The Drug Usage Subcommittee of the Pharmaceutical Benefits Advisory Committee reports on antimicrobial use in the community sector to the Expert Advisory Group on Antimicrobial Resistance, the Australian Institute of Health and Welfare and the World Health Organization International Committee on Drug Statistics Methodology. Antimicrobial usage data are also published in The Australian Statistics on Medicines. The data are used by the National Prescribing Service to inform program planning.

- Australian antimicrobial usage data are incomplete and not linked with resistance surveillance data, which limits their potential use.

A1.1 Recommendations on antimicrobial usage: monitoring and analysis

1. Monitoring of national antimicrobial usage and resistance surveillance data, resistance management, and intervention strategies requires a comprehensive integrated surveillance program.

2. National antimicrobial stewardship guidelines are required for all health-care settings; surveillance data should guide the development and updating of prescribing guidelines, decision support systems (including computerised approval systems), clinical guidelines and education.

3. Antimicrobial resistance and usage data should be made available at clinical service, hospital and national levels.

A1.2 Background

The World Health Organization (WHO) and other international bodies have nominated antimicrobial resistance as a major public health concern. Surveillance of antimicrobial usage and resistance in human and animal populations is widely recommended as part of ongoing management and containment plans.

There is a well-documented causal relationship between prior antimicrobial usage and the emergence of bacterial resistance.[1] The use of particular antimicrobial classes is linked with the emergence of specific pathogens. Chapter 7[a] examines the relationship between prior antimicrobial use and the development of antimicrobial-associated diarrhoea or colitis due to *Clostridium difficile*. Similarly, Chapter 6[b] considers risk factors associated with antimicrobial use for methicillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant *Enterococcus* (VRE) and multiresistant gram-negative organisms.

Monnet proposed three levels of evidence for a link between prior antimicrobial use and resistance,[2] based on an earlier publication by McGowan:[1]

- patient-level data on exposure to antimicrobials, with infection or colonisation by resistant bacteria as the outcome (i.e. case–control analyses)[3-5]

- aggregated, nonlongitudinal data, at one point in time, for a large number of similar and independent settings[6-8]

- aggregated, longitudinal data for a long period of time but for a single ward, hospital, region or country.[9-10]

Multivariate time series analysis is now used to show how month-to-month variation in use of specific antimicrobial classes correlates closely with subsequent variation in antimicrobial resistance (e.g. changes in hospital MRSA incidence).[11] The most instructive example of this method of analysis is the study by Monnet and colleagues,[12] which examined antimicrobial use and the emergence of two particular clones of MRSA in the Aberdeen Royal Infirmary in 1996–2000. Dynamic, temporal relationships were found between monthly prevalence of MRSA in hospitalised patients and MRSA prevalence, and the use of macrolides, third-generation cephalosporins and fluoroquinolones in previous months. Figure A1.1 shows the summed monthly use of macrolides, third-generation cephalosporins and fluoroquinolones (taking into account their respective lags for direct effects) plotted against monthly MRSA prevalence. The parallel nature of the relationship between the lagged use of these specific antimicrobial classes and MRSA prevalence is striking.

The seriousness of the antimicrobial resistance problem in Australia came into national focus in 1998 when the Australian health and agriculture ministers established the Joint Expert Technical Advisory Committee on Antibiotic Resistance

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a In: *Reducing harm to patients from health care associated infection: the role of surveillance.* Eds Cruickshank M, Ferguson J. Australian Commission on Safety and Quality in Health Care, July 2008.

b In: *Reducing harm to patients from health care associated infection: the role of surveillance.* Eds Cruickshank M, Ferguson J. Australian Commission on Safety and Quality in Health Care, July 2008.
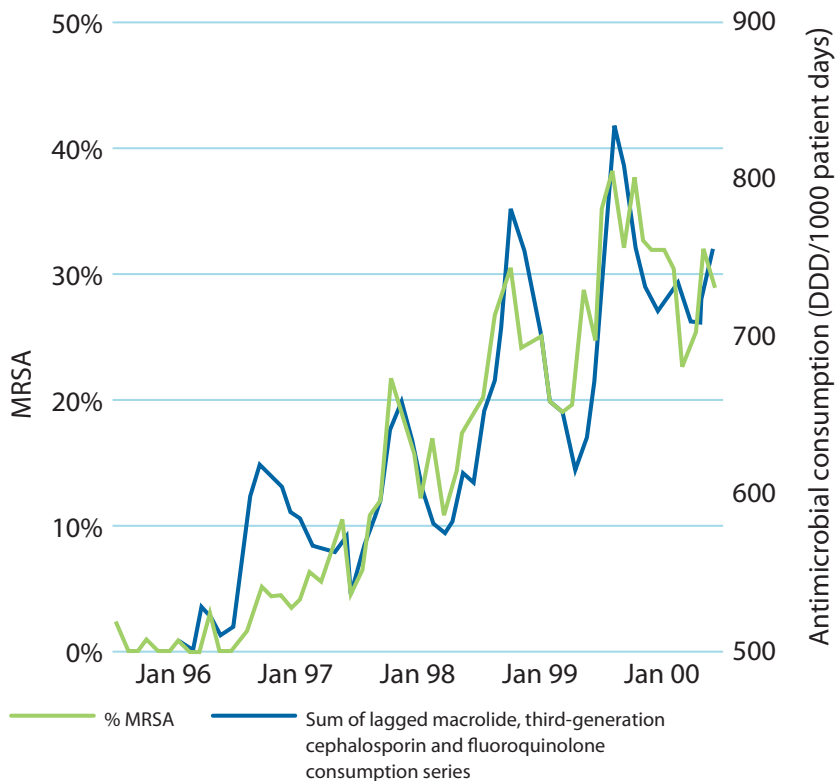
DDD = defined daily dose
The R^2 value describing the overall correlation of these variables with MRSA prevalence was 0.902
Source: Adapted from Monnet et al. (2004)[12]

Figure A1.1 **Evolution of the monthly per cent methicillin-resistant**
Staphylococcus aureus **(MRSA) and monthly sum of lagged**
antimicrobial use as identified in a polynomial distributed
lag model: macrolides (lags of 1–3 months), third-generation
cephalosporins (lags of 4–7 months) and fluoroquinolones (lags
of 4 and 5 months), Aberdeen Royal Infirmary, January 1996–
December 2000

(JETACAR), which includes experts from the health, veterinary and agricultural areas. JETACAR reviewed antimicrobial resistance in Australia; in particular, the evidence that antimicrobial use in food animal production may be contributing to the emergence and spread of resistant bacteria in Australia.[13] The committee recommended an integrated management plan for antimicrobial resistance in Australia including research, monitoring and surveillance, education, infection control, and regulation.

In 2000, in response to the JETACAR report, the Australian Government established an Expert Advisory Group on Antimicrobial Resistance (EAGAR). One of the terms of reference for EAGAR was to provide expert advice on 'the monitoring of antimicrobial use'. Recently, EAGAR commissioned a report to develop the rationale for a comprehensive integrated surveillance program to improve Australia's response to antimicrobial resistance.[14] In line with the previous JETACAR recommendations, EAGAR proposed an integrated surveillance program

coordinating efforts to measure antimicrobial use and resistance in both animal and human settings. Such surveillance data might then drive significant and beneficial change, similar to that seen as a result of the Danish Integrated Antimicrobial Resistance Monitoring and Research Program (DANMAP).[15] The proposed surveillance program would be cross-disciplinary and nationally coordinated, and would consolidate and build on existing surveillance systems and initiatives. Key components of the proposed program for Australia are development and implementation of national surveillance systems for antimicrobials in hospitals and the community.[14] Section A1.4.2 discusses the current status of this program.

Surveillance data on antimicrobial usage provide data that are needed for determining the impact of usage patterns on bacterial resistance. Such data are also important for supporting containment strategies, such as antimicrobial stewardship programs (see Case study 1).

The density of antimicrobial use within specialised units such as intensive care units (ICUs), haematology and oncology units, and solid-organ transplant units is several-fold higher than in other hospital settings. This increased use has been shown to generate high rates of antimicrobial resistance; therefore, these areas should be a particular focus for surveillance and intervention.

Case study 1   Use of ceftriaxone at a South Australian hospital

High usage of third-generation cephalosporins in South Australian metropolitan hospitals was noted in 2002 through data collection and analysis by the South Australian Antimicrobial Usage Surveillance Program. One hospital implemented an antimicrobial restriction policy in January 2003, with a focus on community-acquired pneumonia treatment protocols, which had been identified through pharmacy audit as an area of inappropriate use of ceftriaxone.

Figure A1.2 shows that usage of ceftriaxone decreased significantly following the implementation of the new policy and that this level of use was sustained for about four years. However, ceftriaxone use appears to again be on the rise. This has been at least partly attributed to the lack of input from specialist antibiotic pharmacists in recent years; a followup intervention is being considered.

This case study demonstrates the usefulness of surveillance of antimicrobial use. Surveillance allowed the detection of high usage of a specific group of agents; this stimulated investigation and the implementation of a targeted intervention, which was followed by monitoring of the effect of the intervention.

A1.3 Antimicrobial stewardship programs

A1.3.1 Hospital programs

Antimicrobial stewardship has been defined as 'an ongoing effort by a health-care institution to optimise antimicrobial use among hospital patients in order to improve patient outcomes, ensure cost-effective therapy and reduce adverse sequelae of antimicrobial use (including antimicrobial resistance)'.[16] Stewardship programs aim to change antibiotic prescribing to reduce unnecessary use and promote the use of agents less likely to select resistant bacteria, in line with

guidelines and demonstrated incidence of antibiotic resistance (as shown by antibiograms, an antibiogram being the result of laboratory testing on an isolated pathogen to find out what treatments the pathogen is resistant to). Successful programs have been shown to reduce institutional resistance rates as well as morbidity, mortality and cost.[17]
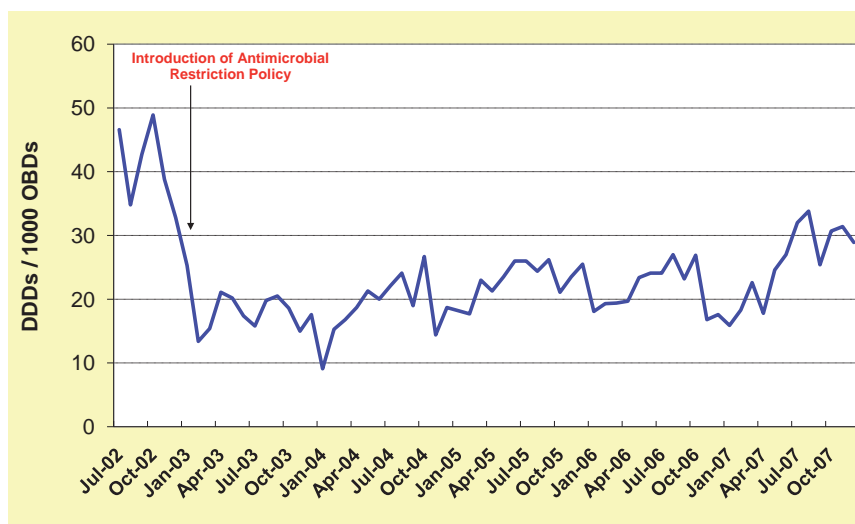
DDD = defined daily dose; OBD = occupied bed-day

Figure A1.2   The usage of ceftriaxone at a South Australian hospital

Minimum requirements for hospital antimicrobial stewardship programs have been set down by the European Society of Clinical Microbiology and Infectious Disease (ESCMID) Study Group for Antibiotic Policies (ESGAP). They detail the responsibilities of clinicians, clinical governance, hospital managers and health-care executives, pharmacies, microbiology laboratories, and pharmaceutical industry members.[18]

Key requirements of an antimicrobial stewardship program include:

• provision of appropriate administrative support for programs

• provision of effective medical education about antibiotic usage and resistance, and responsible prescribing

• implementation of effective clinical guidelines for common infections and promotion of compliance with accepted standards such as *Therapeutic Guidelines: Antibiotic*[a]

• use of clinical decision-support systems — including computerised systems — to promote best evidence-based practice (e.g. Australian systems such as Guidance DS® and IDEA3S®)

• active processes to restrict prescribing of broad-spectrum antimicrobials to those

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a   etg.tg.com.au/complete/

patients where use is clinically indicated

- active regular clinical liaison between clinical microbiologists, infectious disease physicians and pharmacists to improve individual patient management in intensive care and other settings

- close cooperation between microbiology or infectious diseases departments and pharmacy departments to ensure best use of antibiotics

- regular drug usage evaluations (DUEs) under the auspices of each institution's drug and therapeutics committee.

Intervention programs that restrict use of broad-spectrum antibiotics have shown dramatic effects on antibiotic prescribing, as shown, for example, by Case study 1. Some Australian hospitals with antimicrobial stewardship programs have demonstrated significant cost savings through reduction in drug costs; an example is shown in Case study 2.

Computerised decision support systems have been developed and are in use in several Australian hospitals.[19] These systems can reduce the consultation burden for infectious diseases physicians, but it is not clear whether they produce positive patient outcomes overall.[20]

Community programs

In the 1990s, community antibiotic use in Australia was high compared with other developed nations.[21] Today, multiresistant bacteria, such as community strains of MRSA and extended-spectrum beta-lactamase-producing gram-negative bacteria, are causing increasing human morbidity and there is concern that past excessive antibiotic use in the community or in animal production systems (or both) is responsible.

The National Prescribing Service (NPS) delivers programs across Australia that promote judicious antibiotic prescribing in general practice through educational visiting, guideline dissemination, prescribing practice reviews and public education programs. NPS targeting of antibiotic prescribing contributed to a significant decline in antibiotic prescribing over the five year period 1999–2004.[22] In addition, the use of amoxycillin as a proportion of total antibiotic use increased, while use of cefaclor decreased. These changes are consistent with a shift in prescribing towards guideline recommendations.[22]

Comparable programs in veterinary practice are poorly developed.

The NPS also supports drug-usage evaluation programs in hospitals in collaboration with state DUE groups. One such program was Community-Acquired Pneumonia: Towards Improving Outcomes Nationally (CAPTION).[23] This study was a multicentre cross-sectional audit to assess compliance with *Therapeutic Guidelines: Antibiotic*[a] for treatment of community-acquired pneumonia in Australian emergency departments, and

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a   etg.tg.com.au/complete/

occurred between April 2003 and February 2005. Compared with the baseline audit, a 1.5-fold increase in the rate of guideline-compliant antibiotic prescribing was seen.[24]

Case study 2   Effect of active antimicrobial stewardship program in a large tertiary hospital in New South Wales

A large tertiary teaching hospital in New South Wales has had an active approach to antimicrobial stewardship for many years, underpinned by locally relevant antibiotic guidelines and enthusiastic staff in the areas of pharmacy, infectious diseases and microbiology. Clinical teams are regularly engaged in guideline review, development and implementation at local and national levels. Specific discussions about patients are prompted by an online anti-infective registration (approval) system, where clinicians who prescribe broad-spectrum agents register the indication for use and are advised on correct dosage. Twice-weekly infectious diseases and microbiology patient rounds take place in intensive care units (ICUs). These frequently lead to changes in antibiotic therapy, generally to early cessation.

A drug usage evaluation pharmacist regularly audits antibiotic use for particular agents (e.g. meropenem) or clinical syndromes or situations, mainly community-acquired pneumonia and surgical prophylaxis. These audit data are used to provide feedback to clinicians to encourage more appropriate use.

Monthly data on usage are supplied to the National Antimicrobial Utilisation Surveillance Program. This allows for benchmarking of ICU and non-ICU usage against 22 other large Australian hospitals. A study of usage of selected high-cost (predominantly broad-spectrum) antibiotics in 2006 indicated that, for most agents, use in ICU and non-ICU situations in this hospital was far lower than the national average. Based on purchase cost alone, the net cost difference in 2006 was $278,000 ($59,000 of this was for ICU use).

A1.4 Impact on the health-care system

The emergence and selection of resistant bacteria and other organisms driven by inappropriate antimicrobial use and subsequent transmission among hospital patients has a significant impact on morbidity, mortality and treatment costs. This applies to both current and future hospital patients due to changes in hospital microbial ecology resulting from this emergence and selection.

Additional costs of infections caused by resistant organisms include:

•   the need for more expensive antibiotics to treat the infections

•   the need to isolate patients colonised with resistant organisms in order to prevent cross-infection.

Another cost is through inappropriate prescribing of expensive broad-spectrum antibiotics. The existing NAUSP demonstrates unexplained wide variation in usage rates for these agents.[25] While this variation may be due to a difference in patient-mix and acuity, the degree of variation seen across 23 large tertiary hospitals

suggests that different approaches to antibiotic restriction are also responsible. Case study 2 is a good example of the costs and benefits of a successful antimicrobial stewardship program.

If unchecked, high levels of antimicrobial usage increase the pool of patients who are colonised or infected with resistant organisms both in the community and in hospitals.[26] This situation is an important externality that has not yet been captured in economic evaluations of healthcare associated infection (HAI).[27]

A1.5 Surveillance methods

A1.5.1 Measurement

There are two main methods of antimicrobial data collection: patient-level surveillance and population surveillance.[28]

Patient-level surveillance involves collecting data about the dose, dosage interval and duration of therapy for individual patients. This approach gives the most accurate information, particularly if the aim is to link excessive antimicrobial use with development of resistance in a particular area of practice. Such information is usually only available through labour-intensive reviews of drug usage. Electronic prescribing and recording of drug administration will make patient-level surveillance a possibility in the future.

Population-surveillance data refer to aggregate antibiotic use data, and most hospitals supply such data from pharmacy reports, summarised at the level of a hospital or unit. Although possibly not as accurate as patient-level surveillance, population-level surveillance is the only realistic alternative for ongoing and systematic monitoring of antibiotic use. The data are generally derived from the volume of antimicrobial medications issued to wards and clinical units or from individual patient prescription data. The latter method is preferred because it provides a more accurate measure of the quantity used during the data collection period. However, in most hospitals in Australia, comprehensive data at the individual patient level are not available and aggregate data from issues to wards combined with individual patient dispensing records are used. Another data collection method is to use pharmacy purchase data; however, this is less representative than aggregation of ward issues and individual inpatient supplies.

Measurement of community antibiotic use is generally based on prescription data. In Australia, this is collected from two sources: Medicare Australia records of prescriptions submitted for payment under the Pharmaceutical Benefits Scheme (PBS) and Repatriation Pharmaceutical Benefits Scheme; and an estimate of nonsubsidised medicines obtained from an ongoing survey of a representative sample of community pharmacies. These data also include antimicrobials dispensed to outpatients and discharged patients in three states (Queensland, Western Australia and Victoria).

A1.5.2 Definitions

The anatomical therapeutic chemical (ATC) classification system is the international drug classification system recommended by WHO. The ATC code enables reporting at the levels of anatomical group, therapeutic subgroup, pharmacological subgroup, chemical subgroup and chemical substance. The ATC code for antimicrobials is J01.

A defined daily dose (DDD) is the international unit for comparing drug use, as defined by WHO, and corresponds to the assumed average maintenance dose per day for the main indication of a drug in adults.

Use of this internationally accepted standard enables:

*   comparison of the usage of antimicrobial agents with differing doses
*   aggregation of data to assess usage of antimicrobial classes
*   comparison with data from other surveillance programs or studies.

Because DDDs are based on adult dosing, this parameter cannot be used to measure antimicrobial usage in paediatric populations. Age-group specific DDDs are being investigated as a potential standard measure for children.

A1.5.3 Validation

Information about validation of antibiotic usage data collection is scarce. The South Australian program and NAUSP, based in South Australia, implement a system of semi-automated data validation steps before loading contributor data. This database can data map synonymous drug terminology and filter out exclusions such as topical antibiotics.

A1.5.4 Reporting

Hospitals

Usage in DDDs is calculated from the quantity of antimicrobial used and reported by antibiotic type or class (ATC subgroup). These data are used to produce an aggregate measure of total usage. Intensive care usage is generally reported separately.

To facilitate comparisons, DDD data are normalised into usage density rates, which are calculated as follows, where OBDs are occupied bed-days:

$$\text{Usage density rate} = \frac{\text{No. of DDDs/time period}}{\text{OBDs/time period}} \times 1000$$

OBD has been widely accepted as the most appropriate denominator in the non-ambulatory (hospital) setting and has been adopted by most international programs. Antimicrobial usage data for outpatient areas, including hospital-in-the-home, day-treatment centres, day surgery and dialysis clinics, are variably excluded from some surveillance programs to ensure that data correspond to OBDs.

Standard methods for reporting usage in paediatric groups have not been established. In neonatal intensive care, measures (stratified by birthweight or gestational age cohorts) that have been reported include the proportion of: [29-31]

- admitted patients who receive an antibiotic course

- patient days that the patient receives antibiotics

- patient days that the patient receives a specific antibiotic (e.g. vancomycin).

Community

In Australia, the Drug Usage Subcommittee of the Pharmaceutical Benefits Advisory Committee (PBAC) uses number of prescriptions and DDD per 1000 population per day as units of drug usage measurement.[32]

Future report formats

Statistical analysis of variation over time through use of control charts or time series analysis is advisable. This enables detection of potentially significant changes in usage rates. Morton and Looke[33] discuss the use of generalised additive models for the production of antibiotic use control charts. These enable better identification of out-of-control usage at a facility level. It is not known how useful aggregated reporting is at a national level.

Use of time series analysis with transfer-function analysis enables statistical examination of seasonal and other variations as a prelude to correlation of usage with antibiotic resistance[10] (see Figure A1.1a).

A1.6 Current surveillance systems and data

A1.6.1 International

Europe

A number of surveillance programs have been initiated in Europe during the past decade with an increasing focus on detailed descriptions of patterns of:

- antimicrobial consumption in both hospital and community settings

- resistance in

  » zoonotic bacteria

  » specific (targeted) human pathogens

  » bacteria from diagnostic samples (human and animal).

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a In: *Reducing harm to patients from health care associated infection: the role of surveillance.* Eds Cruickshank M, Ferguson J. Australian Commission on Safety and Quality in Health Care, July 2008.

Many of these programs have been developed since the European Union conference, *The Microbial Threat*, held in Copenhagen in 1998, where it was agreed that antimicrobial resistance was an international issue and required a common European strategy. A progress report was submitted in June 2001 summarising the status of various activities, obstacles encountered and considerations for the future.[34] A further report detailing progress and proposals for future action was submitted in late 2005.[35]

The European Surveillance of Antimicrobial Consumption program (ESAC) was launched in November 2001 to establish a system for standardised collection, analysis and interpretation of data on antibiotic consumption. The ESAC program includes data from 34 countries, including European Union states and other central and Eastern European countries. The initial phase of the ESAC project includes data on human antibiotic consumption and resistance only and reports rates representing total community use for each region, with aggregate hospital usage data also generated where available. A database accessed via a web site is planned to allow continuous and standardised updates and exchange of internationally comparable data for benchmarking between contributors and other countries. Future initiatives include:

- agreement on evidence-based guidelines for therapeutic and prophylactic human use

- agreement on threshold resistance levels for total cessation of use of particular antimicrobial agents

- development and assessment of intervention strategies to improve antimicrobial prescribing in hospitals and the community

- improved patient education on antimicrobial use.

A corresponding program — European Antimicrobial Resistance Surveillance System (EARSS) — coordinates surveillance of antimicrobial resistance.

The ARPAC (Antibiotic Resistance; Prevention and Control) project established a network of European hospitals and recommended collation of data on antibiotic use. The project ran from January 2002 to June 2005, with work being carried out by four study groups under the auspices of ESCMID. ARPAC recommended that whole-hospital antibiotic usage data, categorised by class, should be recorded quarterly using the WHO-defined unit of DDD per 1000 patient days and the ATC classification system.[36]

The project CARE-ICU (Controlling Antibiotic Resistance in ICUs) was piloted in 2005 through funding from the European Commission. This project enabled the continuous monitoring of antibiotic use and resistance with automatic feedback through a web site. Antibiotic usage was expressed as DDD/1000 bed-days.[37]

Denmark

DANMAP is a collaborative, ongoing program involving the Danish Veterinary Laboratory, Danish Veterinary and Food Administration, Statens Serum Institute and the Danish Medicines Agency. It is the best long-standing example of an integrated country-wide approach to surveillance. DANMAP was established in 1995 to collect data and report trends in resistance in pathogenic bacteria and in the use of antimicrobial agents in food animals and humans. The Danish Medicines Agency has legal responsibility for monitoring consumption of all human medicines; it receives data on all antimicrobial issues from community pharmacies (since 1994) and hospital pharmacies (since 1997). Consumption data from monthly reports from all Danish pharmacies, including hospital pharmacies, is provided to the Danish Medicines Agency. Annual reports have been produced since 1996.[9, 15]

Other European countries

The Netherlands, Sweden and Germany have established antimicrobial surveillance programs in response to increases in antibiotic resistance. All programs collect data on human antimicrobial consumption and resistance rates. In the Dutch program, NethMap (surveillance program for antimicrobial resistance in the Netherlands), in-hospital usage data are provided for antibiotics used systemically; data are provided by ATC classification in DDD per 1000 patient days and DDD per 1000 admissions.[38]

The Swedish Strategic Program for Rational Use of Antibiotics (STRAMA) was established in 1995. It produces an annual report — Swedish Antibiotic Utilisation and Resistance in Human Medicine (SWEDRES) — that includes data on total antibiotic use in terms of DDD per 1000 population per day and prescriptions per 1000 per day, and hospital use as DDD per 100 patient days and DDD per 100 admissions. ICU data are collected separately. Data from 2001 to 2006 are available.[39] STRAMA provides the web site application for the European Union CARE-ICU project.

In Germany, the SARI project (Surveillance of Antimicrobial Use and Antimicrobial Resistance in ICUs) collected data on the use of antimicrobials in ICUs from 2001 to 2004. Consumption was expressed as DDD per 1000 patient days.[40]

United States

Project ICARE (Intensive Care Antimicrobial Resistance Epidemiology) started in 1996. It provides data on the prevalence of antimicrobial resistance, and use, in a subset of hospitals participating in the United States National Healthcare Safety Network (formerly the National Nosocomial Infections Surveillance System) system of the United States Centers for Disease Control and Prevention.[41] A DDD was designated and usage density rates were provided as number of DDD per 1000 patient days. Unfortunately, the DDDs used were not consistent with the WHO definitions.

A1.6.2 Australia

Hospital usage

South Australia

A state-wide antimicrobial usage surveillance program was established in November 2001 as an initiative of the Infection Control Service, Communicable Disease Control Branch and the Pharmaceutical Services Branch of the South Australian Department of Health in response to recommendations arising from the JETACAR report. This program now collects in-hospital antimicrobial usage data from metropolitan and country hospitals and private and public hospitals.

Complete usage data from November 2001 are available for eight metropolitan hospitals. Four additional metropolitan hospitals have provided data since 2002 and one more since 2003, making a total of 13 metropolitan contributors. This group includes seven public and six private hospitals, ranging in size from about 100 to 650 beds. Stratification by hospital type or size has been avoided due to the limited number of contributors. ICU usage rates are reported for five hospitals (three public and two private). Accurate ICU data are not available for a number of small units and total hospital usage is reported for these hospitals.

Contributing hospitals submit antimicrobial consumption and bed occupancy data on a monthly basis. Each hospital is sent monthly reports detailing antimicrobial usage density rates within that hospital. DDDs, as defined by WHO, are used for all rate calculations. Usage rates for six antibiotic classes, and for individual agents within those classes, are routinely reported to each contributor. Reports are presented as time series graphs, generated automatically by a custom-built database. Corresponding 'state-wide' rates, calculated from aggregate data, are also supplied for comparison. Usage rates for other classes or agents can be extracted from the purpose-built database as required. Specific usage rates for ICUs are also supplied where data are provided. Routine monthly reports are distributed to hospital executive officers, specialist antimicrobial or drug committees, infection control committees and pharmacy directors. Separate reports detailing monthly usage rates within ICUs are supplied to unit directors on a quarterly basis.

Several country hospitals submit data, and individual reports are generated, but the data are not aggregated due to the diversity among these hospitals and the lack of a suitable benchmark for smaller hospitals.

State-wide aggregate reports are publicly available from the Infection Control Service web site.[a]

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a www.health.sa.gov.au/infectioncontrol

Queensland

The Centre for Healthcare Related Infection Surveillance and Prevention (CHRISP) provides Queensland Health, and other interested organisations, with information on the epidemiology, economics and prevention of HAIs. CHRISP is developing a program to monitor antimicrobial usage data for all Queensland Health facilities based on data extracted from the state-wide pharmacy database. Monthly state-wide reports will be available on the Queensland Health intranet and detailed reports from the database will be available to Queensland Health infectious diseases physicians, microbiologists, pharmacists and infection control practitioners. The reports will provide evidence to better support local antimicrobial stewardship programs.

The main emphasis of the reporting is longitudinal analysis of data within a facility or district. Improvement of the existing antibiogram system is also planned to provide clinicians with efficient access to state-wide and local antibiograms and antibiotic resistance data. CHRISP intends to correlate antimicrobial usage with antibiograms by extracting data from pharmacy and pathology systems. The aim is to identify and quantify the effects of antimicrobial prescribing habits on antibiotic resistance.

Other states

There are no other state-based antibiotic usage monitoring programs in Australia.

National

NAUSP, which was based on the South Australian program, started in July 2004. It is funded on an annual basis by the Australian Government Department of Health and Ageing. Data are processed using the South Australian database, which is currently being redeveloped to be able to accept a larger number of contributors and provide improved reporting capabilities, including statistical analysis.

In-hospital antimicrobial usage data are collected from 23 tertiary referral hospitals from all states except Queensland. This represents 50% of Australian principal referral hospitals. Hospitals range in size from about 300 to 700 adult acute-care beds. Monthly reports, as described earlier for South Australia, are provided electronically to nominated infectious diseases physicians, clinical microbiologists and pharmacy representatives at these hospitals. ICU usage rates are currently reported for 21 level 3 units (i.e. tertiary ICUs). Where ICU data cannot be supplied, total hospital usage is reported. Corresponding 'national' rates, calculated from aggregate data, are included for comparison.

Analysis of usage data for NAUSP from July 2004 to June 2007 shows a slight decrease in total aggregate antibiotic consumption. However, there are both upward and downward trends in usage of individual antibiotic classes and agents within classes. Increasing usage has been demonstrated in some hospitals, providing targets for possible intervention programs.

The data on national antibiotic use surveillance also highlight priorities for change and the potential to document the effect of future multicentre interventions.[25]

Quinolone usage is a risk factor for hospital MRSA[12, 40, 42-43] as well as antimicrobial resistance in various gram-negative organisms.[44-45] Figure A1.3 shows increasing use of the quinolone ciprofloxacin in Australian hospitals between July 2004 and June 2007. Increases in total ciprofloxacin use between 2005–06 and 2006–07 have been demonstrated at 10 of 21 sites, with increases of greater than 30% at two sites.
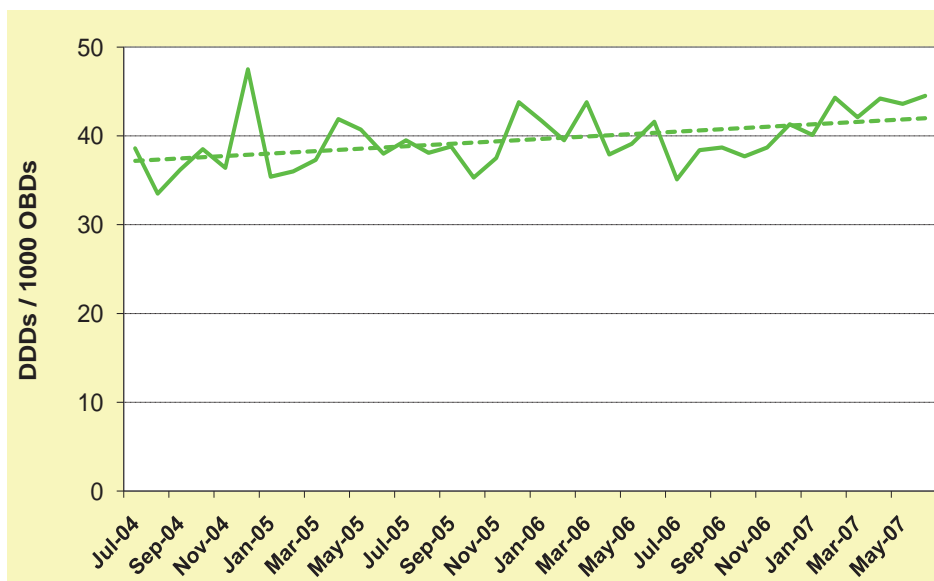
DDD = defined daily dose; OBD = occupied bed-day
Source: National Antimicrobial Utilisation Surveillance Program, Annual Report 2006–07[25]

Figure A1.3   Usage of ciprofloxacin between July 2004 and June 2007 by National Antimicrobial Utilisation Surveillance Program contributors

The aggregate rate for total antibiotic usage for 2006–07 was 916 DDDs/1000 OBDs compared to 928 for 2005–06 and 939 for 2004–05. For ICUs, the aggregate rate was 1658 DDDs/1000 OBDs in 2006–07, a slight decrease from the figure of 1684 in 2005–06.

Comparison with international data demonstrates that Australian usage rates in the contributing hospitals remain high for some antibiotic classes (see Figure A1.4[a]). This may be related to the incidence of particular infections, prescribing policies and drug availability. Total aggregate antibiotic usage rates for the 23 Australian hospitals for which data have been analysed were 916 DDDs/1000 OBDs compared with 649 DDDs per 1000 OBDs for Denmark,[9] 583 DDDs per 1000 OBDs for the Netherlands[46] and 589 DDDs per 1000 OBDs for Sweden.[47]

Although the current national data collection is limited to 50% of tertiary referral hospitals, it has laid the groundwork for the establishment of a comprehensive national surveillance program for hospital antimicrobial drug use.

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a In: *Reducing harm to patients from health care associated infection: the role of surveillance*. Eds Cruickshank M, Ferguson J. Australian Commission on Safety and Quality in Health Care, July 2008.

The 2006 EAGAR report specified the requirements of a comprehensive national surveillance system for hospitals as follows:[14]

- a generic computer program capable of accepting antimicrobial usage data from individual hospitals from all states and territories
- automated analysis of the data with production of reports and charts that provide individual hospital, state and national usage rates.

Data generated from the system would be used to:

- enable examination of trends in hospital antimicrobial use at state and national levels as the basis for larger-scale interventions to rationalise hospital antimicrobial prescribing
- evaluate the impact of interventions in the hospital setting at local, state and national levels
- produce longitudinal antimicrobial usage data that could be used to demonstrate a link between antimicrobial use and future development of resistance, both at local hospital and national levels
- provide an Australian peer group benchmark for comparison and enable comparison with international data
- inform antimicrobial stewardship programs and monitor intervention strategies.

NAUSP currently fulfils most of these requirements. However, it needs to be expanded, with appropriate resourcing, to include data from all tertiary hospitals and selected smaller hospitals and to include reporting by hospital peer group with appropriate case-mix adjustment. Reporting should also be expanded to include usage by specific clinical specialties and within area health regions.
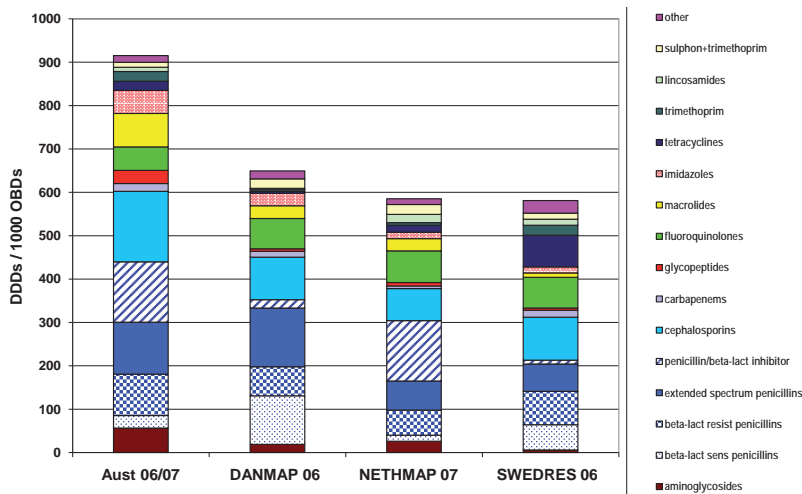
Aust = Australia; DANMAP = Danish Integrated Antimicrobial Resistance Monitoring and Research Program; DDD = defined daily dose; NethMap = surveillance program for antimicrobial resistance in the Netherlands; OBD = occupied bed-day; SWEDRES = Swedish Antibiotic Utilisation and Resistance in Human Medicine

Source: National Antimicrobial Utilisation Surveillance Program, Annual Report 2006–07[25]

Note: NethMap 07 is based on 2005 data. SWEDRES 06 is based on 2005 data.

Figure A1.4   Comparison of aggregate antibiotic usage rates in Australian hospitals with international benchmarks

Community usage

The consumption data on community antibiotic usage collected by the PBAC Drug Usage Subcommittee is reported biennially in *Australian Statistics on Medicine*. Information on this type of data collection is given in Section A1.3.1[a]. The data are reported at a national level and can be provided at the state level; they can be obtained directly from the Drug Usage Subcommittee. Antibiotic usage data are routinely monitored by the Drug Usage Subcommittee and periodic reports are sent to EAGAR. Annual reports are provided to the Australian Institute of Health and Welfare (AIHW) and to the WHO International Committee on Drug Statistics Methodologies. As explained, these data also include antimicrobials dispensed by hospital pharmacies to outpatients and discharged patients in three Australian states. The volume of data will increase as more states implement the pharmaceutical reforms that allow dispensing of PBS prescriptions for outpatients and on discharge.

The Drug Usage Subcommittee also reports to government on the prescription rate for oral antibiotics most commonly used to treat upper respiratory tract infection. This is reported for individual states and Australia-wide. Due to data restrictions, the report is based only on PBS concession card holders.

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a   In: *Reducing harm to patients from health care associated infection: the role of surveillance.* Eds Cruickshank M, Ferguson J. Australian Commission on Safety and Quality in Health Care, July 2008.

The total use of antibiotics in the Australian community falls in the middle of the range recorded in European countries: in 2002, Australian community antibiotic use was 21 DDDs per 1000 population per day.[32] Usage was highest in France at 32 DDDs/1000/day, while the Netherlands had the lowest usage at 10 DDDs/1000/day.[48-49]

The Bettering the Evaluation and Care of Health project (BEACH) of the Australian General Practice Statistics and Classification Centre[a] collects data on clinical activities in general practice. These data include medications (prescribed, advised and provided), clinical treatments and procedures provided. As of July 2007, there were 90 000 general practitioner encounters in the database. BEACH reports on rates of prescribing; it also contributes to AIHW reports.[50] Data from the BEACH project demonstrated a significant decline in antibiotic prescribing in general practice over the five-year period 1999–2004.[86] No comprehensive resistance data were available to monitor the effect of this decline. Prescribing for upper respiratory tract infections decreased during that period from 42% of patient general practitioner visits for upper respiratory tract infections in 1998–99 to 35% in 2002–03.[50] This change represented a shift towards recommended management as promoted through NPS-targeted interventions.[22]

In 2004, antibiotic prescriptions began to increase again. An increase in doctor visits for respiratory tract infections and the ability of Queensland hospitals to directly access the PBS for outpatient and discharge prescriptions from early 2004 may have contributed to this increase. The increase was mainly in penicillins (amoxicillin), which indicates continuing adherence to NPS recommendations. Rates now appear to have stabilised at a rate less than that of 2001.[32]

Future developments should include integrating the antimicrobial usage data from all care sectors (primary through to tertiary) and linking usage data with resistance patterns in a similar manner to DANMAP.

a   www.fmrc.org.au/beach.htm

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2 Resource materials

A2.1 Examples of committee terms of reference, policies, guidelines and educational materials from Australian hospitals

Disclaimer: The Australian Commission on Safety and Quality in Health Care does not warrant the content of the materials in this section. They are provided as examples only. They may contain therapeutic recommendations that are not consistent with the latest version of *Therapeutic Guidelines: Antibiotic.*[19]

Additional antimicrobial stewardship resources are available from the ACSQHC web site www.safetyandquality.gov.au/internet/safety/publishing.nsf/Content/PriorityProgram-03#five

Australian hospitals

Southern Health

Antimicrobial Management Program at Southern Health (AMPS)

Program Meetings
TERMS OF REFERENCE

Background

The Antimicrobial Management Program (AMPS) will operate across all Southern Health campuses and aims to review and optimise clinical outcomes of antimicrobial use while minimising unintended consequences including: toxicity; under or overdosing; inappropriate antimicrobial selection and emergence of resistant organisms.

The appropriate use of antimicrobials is a critical component of patient safety and deserves careful management and guidance. The combination of an effective antimicrobial management program with a comprehensive infection control program has been shown to be a cost effective measure in limiting the emergence and transmission of antimicrobial resistant bacteria.

Role

The role of the AMPS team will be to:

- Conduct prospective audit with intervention and feedback;
- Review and implement formulary restrictions and preauthorisation;
- Develop antibiotic policies;
- Provide education to pharmacy, medical and nursing staff to impart a foundation of antimicrobial knowledge in order to enhance acceptance;
- Update, develop and implement clinical practice guidelines for antimicrobial treatment and prophylaxis;
- Promote streamlining or de-escalation of therapy on the basis of culture results;
- Introduce automatic stop orders;
- Optimise antimicrobial dosing based on individual patient characteristics, the causative organism, site of infection as well as pharmacokinetic and pharmacodynamic parameters;
- Encourage parenteral (IV) to oral conversion when appropriate;
- Implement an electronic antimicrobial approval system to improve antimicrobial decisions through the provision of clinical decision support;
- Provide clinical microbiology data to enable targeted antimicrobial selection and optimisation of individual treatment regimens as well as assist infection control efforts in the surveillance of resistant organisms;
- Take action to reduce the incidence of nosocomial infections and resistance;
- Review antimicrobial prescribing practice against national usage data;
- Promote efficient and cost effective prescribing practices;
- Promote accountability of treating units who fail to obtain Infectious Diseases approval for restricted antimicrobials.

Membership

Infectious Diseases Physician
Clinical Microbiologist
Surgeon
Director of Pharmacy
Clinical Pharmacist with infectious diseases training
Infection Control nurse representative
Executive medical sponsor (as required)
Information system specialist (as required)

Responsibilities

- To oversee antimicrobial use at Southern Health and apply appropriate interventions in order to reduce inappropriate use of broad spectrum antimicrobials.
- To reduce hospital acquired resistance and reduce other unintended consequences of antimicrobial use.

Reporting

The AMPS will report to the Therapeutics Committee and provide minutes to the Joint Programs Quality and Safety Committee (JPQSC).

Meeting Frequency

TBA

Minutes

Pharmacist

SH Strategic Policy	Quality and Risk Management	**ACHS Function**	Leadership and Management
Reviewer	Antimicrobial Management Program Committee	**Last review date**	March 2009
Authoriser	Chair of Antimicrobial Management Program	**Next review date**	March 2012

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Government of South Australia
Children, Youth and Women's
Health Service

PROCEDURE:
Antimicrobial Agents Requiring Infectious Diseases Approval

POLICY:
Individual Health Care – Care Planning and Delivery

PROCEDURE STATEMENT	
Intent:	The intent of this procedure is to provide all prescribers antimicrobial agents with information about the procedures required to gain approval from Infectious Diseases staff to prescribe certain restricted antimicrobial agents. This procedure applies to all prescribers (medical, dental and nursing staff) of systemic and some topical antimicrobial agents in the Children's Youth and Women's Health Service. It does not cover the use of most of the topical antimicrobials.
Exceptions:	None.
Definitions and Acronyms:	**Antimicrobial agent:** any therapeutic substance designed to treat an infection by directly inhibiting the replication of the pathogen causing that infection. It includes antibacterial, antimycobacterial, antiprotozoal, anthelminthic, antifungal and antiviral (including antiretroviral) agents. **Prescriber:** any medical, dental or nursing practitioner approved by CYWHS to prescribe therapeutic substances. **Infectious Diseases Staff:** Registrar and Consultants from the Microbiology and Infectious Diseases Department, Division of Laboratory Medicine. **Department:** Specialty within a clinical Division of CYWHS. **ID:** Infectious Diseases.
Related Forms, Records and Electronic Databases:	• CYWHS Medication Sheet. • CYWHS Outpatient Prescription Form. • Intranet – Drug Info – Therapeutic Guidelines (eTG).
Supporting Procedures/ Protocols/Flow Charts etc:	• Laminated Card – WCH Antibiotic Guidelines.
Key Words:	Antimicrobial, antibiotic, prescribing.

DETAILED STEPS, PROCEDURES AND ACTIONS	
Procedure	**Responsibility**
1. Objectives	
The importance of a hospital adhering to defined antimicrobial agent (antibiotic) prescribing practices is internationally accepted. The objectives are to minimise the selection of antibiotic-resistant organisms, promote safe and effective antibiotic prescribing, minimise unnecessary prescribing and prevent unnecessary expenditure. Of these, the most important is the selection and amplification of resistant organisms. Inappropriate prescribing (e.g. the use of an agent when none is required, or the selection of an incorrect agent, dose, combination or duration) is wasteful and may endanger patient wellbeing. It may also have infection control and public health implications as antimicrobial use can promote the spread resistant bacteria to from person to person, and resistance genes from species to species. The aim of this procedure is to optimise rational prescribing of antimicrobial agents in the Children's Youth and Women's Health Service. As part of achieving this aim, certain antimicrobial agents have been given the status of restricted availability to prescribers. These agents will only be made available from Pharmacy after approval by Infectious Diseases medical staff. Some restricted antimicrobial agents are pre-approved for specific Departments for listed indications. In making the selection of what agents should be restricted, the following points have been considered: spectrum, safety, prevalence of resistance, resistance-inducing and amplification potential, frequency of indication, potential patient hypersensitivity and cost.	
2. Basis for Decisions and Approvals	
The primary basis for decision-making approval is the latest edition of the Therapeutic Guidelines–Antibiotic (13th), a thoroughly researched, peer-reviewed, national standard for empirical and directed antimicrobial therapy using the latest published evidence. Where these guidelines do not provide guidance, available literature is used to assist in defining the most rational therapy. It is considered good medical practice at the CYWHS to collect appropriate specimens whenever possible PRIOR to the commencement of empirical antimicrobial therapy. The following factors are important in determining the list to which agents are allocated: – Known WCH epidemiology of resistance. – Known risks of selective pressure with different antimicrobial classes. – Pharmacoeconomic considerations. – Training and skill level in quality use of antimicrobials by specialities outside ID. (Frequency of interaction between ID and specialty is relevant here).	
3. Procedural Guidelines for Prescribers	
3.1 The following agents must be approved by the Infectious Disease Registrar or Consultants. Where the need for such agents arises, medical staff must contact the Infectious Diseases Registrar (in hours) or Consultant on service (in and after hours), who will determine the appropriateness of the request and either approve the request or endorse an alternative antimicrobial agent. If the requested agent is approved by Infectious Diseases, the prescription or drug chart (in the "Additional Information" box) must be endorsed by the prescriber with **"Approved by (name of ID person)"**.	PRESCRIBER
3.2 *The A List: Agents frequently requested but always requiring ID approval.* The words **"Approved by..."** should appear on the script • Meropenem. • Liposomal amphotericin B or other lipid formulations of amphotericin B.	PRESCRIBERS/ PHARMACY STAFF

3.3	***The B List: Agents with pre-approval for use by nominated departments for listed indications.*** These agents can be prescribed by the nominated clinical departments for the listed indication without the need to seek approval or to endorse the medications chart/prescription. Pharmacy staff are not required to confirm that the antibiotic is for the requested indication. Instead, the indications listed will be used for auditing purposes. If the antimicrobial agents on the B List are requested by other clinical departments, Infectious Diseases approval is required and the words **"Approved by..."** should appear on the medications chart or prescription. The listed indications for pre-approved departments do not require confirmation by Pharmacy staff; they will be used for audit purposes only. Cefepime pre-approval in Oncology for febrile neutropenia Ceftriaxone or Cefotaxime pre-approval in PED, Paediatric General Medicine, PICU, Pulmonary Medicine and Neonatology for (1) Severe pneumonia (2) Moderate to sever periorbital (preseptal) and orbital cellulitis (3) Presumptive occult bacteraemia (PED protocol) (4) Presumptive or proven bacterial meningitis, or severe community-acquired sepsis and meningitis not excluded (5) Nosocomial neonatal sepsis Ceftazidime pre-approval in Pulmonary Medicine for cystic fibrosis patients only Ciprofloxacin oral pre-approval in (1) Pulmonary Medicine for cystic fibrosis patients only (2) Oncology for patients with febrile neutropenia Ciprofloxacin ear drops pre-approval in ENT for chronic suppurative otitis media or otitis externa in the presence of perforated tympanic membrane or grommets. Ciprofloxacin eye drops pre-approval in Ophthalmology for sight-threatening eye infections Colistin inhaled and IV pre-approval in Pulmonary Medicine for cystic fibrosis patients only Fluconazole pre-approval in Neonatology for neonates with serious fungal disease and Oncology and Immunology for the treatment and prophylaxis of serious fungal disease Itraconazole pre-approval in Pulmonary Medicine for cystic fibrosis patients and Oncology and Clinical Immunology for treatment and prophylaxis of serious fungal disease Pentamidine pre-approval for Oncology and Clinical Immunology for Pneumocystis treatment and prophylaxis Piperacillin-tazobactam pre-approval in Oncology for patients with febrile neutropenia and mucositis Rifampicin pre-approval by protocol in PED for meningococcal prophylaxis Vancomycin pre-approval in PICU and Neonatal ICU for patients with presumptive line sepsis, Oncology for patients with febrile neutropenia, PED/General Paediatrics for possible/proven pneumococcal meningitis, and Neurosurgery for possible shunt meningitis Voriconazole pre-approval for Oncology for patients with non-responsive febrile neutropenia	PRESCRIBERS/ PHARMACY STAFF

3.4	*The C List: Other infrequently requested agents always requiring ID approval.*		PRESCRIBERS/ PHARMACY STAFF

The words **"Approved by..."** should appear on the medication chart or prescription.

Antibacterials
    Amikacin
    Chloramphenicol IV
    Ciprofloxacin IV
    Ertapenem
    Fusidic acid
    Imipenem
    Linezolid
    Moxifloxacin
    Ofloxacin topical
    Quinupristin-dalfopristin
    Spectinomycin
    Spiramycin
    Teicoplanin
    Tigecycline
    Vancomycin oral

Antimycobacterials
    Capreomycin
    Clofazimine
    Cycloserine
    Dapsone
    Ethambutol
    Isoniazid
    Prothionamide
    Pyrazinamide
    Rifabutin
    Streptomycin

Antiprotozoals
    Atovaquone
    Chloroquine
    Diloxanide furoate
    Mefloquine
    Pentamidine (except
     Oncology)
    Primaquine
    Proguanil
    Pyrimethamine
    Quinine
    Sulfadiazine
    Sulfadoxine-pyrimethamine

Anthelminthics
    Albendazole
    Diethylcarbamazine
    Ivermectin
    Praziquantel
    Thiabendazole

Antifungals
    Caspofungin
    Flucytosine
    Ketoconazole (oral)
    Posaconazole

Antivirals
    Cidofovir
    Entecavir
    Famciclovir
    Foscarnet
    Ganciclovir
    Oseltamivir
    Ribavirin
    Valaciclovir
    Valganciclovir
    Zanamivir

Antiretrovirals – all

4.1	On receipt of drug chart/script request for one of the agents requiring approval: **For inpatients** 1. Check for **"Approved by...."** if on the A or C List, or prescribed by Infectious Diseases, or if on the B List from a pre-approved department. (Pharmacy staff do <u>not</u> have to confirm that the indication is appropriate; the indications on the B List will be used for audit purposes only.) 2. If Yes, dispense. 3. If No, page ID Registrar in hours (Pager 18048) or Consultant after-hours (through Switchboard who has the roster) and ask them to contact prescriber. ID Registrar/Consultant will ring back with "Approved" or otherwise, which will be documented by Pharmacy staff. 4. Fax (ext. 16051) all **"Approved by..."** drug charts/scripts to Micro/ID Department on a daily basis (for audit purposes). Micro/ID Registrar and Consultants will keep a record of what and for whom they have given approval. Those from the B List <u>that are pre-approved</u> do not need to be faxed; only those B List agents with **"Approved by..."**	PHARMACY STAFF
4.2	**For outpatients on the B List** 1. Dispense. 2. Fax (ext. 16051) drug chart/script to Micro/ID Department on a daily basis. 3. ID will follow-up with prescriber verbally or by written communication.	PHARMACY STAFF
4.3	**For outpatients on the C List** 1. DO NOT DISPENSE. 2. Page/contact prescriber and request referral to ID. If no response within 5 minutes, dispense, and fax script to Micro/ID Department.	PHARMACY STAFF
4.4	**B List Drugs by Pre-Approved Department**	PHARMACY STAFF

	Cefepime	Ceftriaxone or cefotaxime	Ceftazidime	Ciprofoxacin oral	Ciprofoxacin topical	Colistin	Fluconazole	Itraconazole	Pentamidine	Piperacillin-tazobactam	Rifampicin	Vancomycin	Voricoazole
Oncology	√				√		√	√	√	√		√	√
PED and General Paediatrics		√									√	√	
PICU		√										√	
Neonatology		√					√					√	
Neurosurgery												√	
Pulmonary Medicine		√	√	√		√			√				
ENT					√								
Ophthalmology					√								

5.	Procedural Guidelines for Infectious Diseases Staff	
5.1	In hours, the Infectious Diseases Registrar and the on-service Infectious Diseases Consultant will be available to take calls from prescribers and pharmacists, for queries or requests to prescribe agents if they are (i) on the A or C List, or (ii) on the B List and not from an approved unit. After hours, the on-service Infectious Diseases Consultant is available to take such calls. The on-service Registrar or Infectious Diseases Consultant will contact any prescriber who has not followed the procedures listed at their earliest convenience should the antibiotic need to be dispensed (e.g. outpatients). The ID Registrar and on-service ID Consultant will keep a record of verbal approvals. On at most a weekly basis, the on-service Consultant will review approvals sent from Pharmacy. On a less frequent but regular basis, the ID service will audit individual B List approved units for adherence to the listed indications.	INFECTIOUS DISEASES STAFF
6.	Training	
6.1	The contents of this procedure will be promulgated by Infectious Diseases staff to prescribers and Pharmacy staff through meetings, education sessions and at orientation.	INFECTIOUS DISEASES STAFF
7.	Maintenance of Records	
7.1	Medication charts will be retained in the medical records.	MEDICAL RECORDS
7.2	Outpatient prescriptions with approvals and non-compliant with this procedure will be retained by Pharmacy.	PHARMACY STAFF
7.3	Records of approvals and non-compliant requests will be retained for review and auditing by Infectious Diseases staff.	INFECTIOUS DISEASES STAFF
ACCOUNTABILITY		
Effectiveness of this Procedure:	• Regular audits of compliance with this procedure will be undertaken by Infectious Diseases staff, and reported to the Drug and Therapeutics Committee on at least an annual basis.	

St. Vincent's Hospital Antibiotic Policy

St. Vincent's Hospital has an Antibiotic Policy. Antibiotics are classified as either Red, Orange or Green drugs, with each colour representing a certain level of restriction for use within the hospital. When selecting an antimicrobial agent, the prescriber must ascertain the status of the drug. The table below outlines the three groups of antibiotics and lists the drugs in each colour group. The steps required to access restricted drugs are listed in each of the columns. Contact the Microbiology registrar, page 6890, or ward pharmacist if you have any questions.

GREEN ANTIBIOTICS:

Antibiotics are *GREEN* when:

1. The drug is prescribed according to the "Therapeutic Guidelines - Antibiotic 13th Edition" and/or
2. The drug is prescribed within the SVH Indications (overleaf).

Under these circumstances the antibiotic does not require a Microbiology approval number before it is prescribed and dispensed.

See Therapeutic Guidelines - Antibiotics 13th Edition for further details about infections and antibiotic choice, OR contact the Microbiology department.

ORANGE ANTIBIOTICS:

ORANGE antibiotics may be prescribed according to the SVH Indications (shown overleaf) without a Microbiology approval code. The antibiotic is then classified as a green antibiotic (see green column). In **ALL** other situations a Microbiology approval code will be required as for red antibiotics (see red column).

- Aciclovir IV
- Amikacin
- Azithromycin IV/PO
- Cefepime
- Ceftriaxone / Cefotaxime
- Ciprofloxacin IV/PO
- Clarithromycin
- Fluconazole IV
- Sodium Fusidate
- Itraconazole
- Piperacillin + Tazobactam (Tazocin®)
- Ribavirin (SAS)
- Teicoplanin
- Terbinafine
- Ticarcillin + Clavulanate (Timentin®)
- Valganciclovir
- Vancomycin IV/PO

RED ANTIBIOTICS:

All *RED* antimicrobial agents must have **prior** Microbiology approval before they can be prescribed and supplied at SVH. An approval code, which is valid for a specified period, will be issued by the microbiology department and must be included on the medication chart.

- Amphotericin (liposomal and phospholipid complex)
- Caspofungin
- Linezolid
- Meropenem
- Moxifloxacin
- Pristinamycin (SAS)
- Tigecycline
- Voriconazole

8th July 2009

ORANGE ANTIBIOTIC	GREEN INDICATIONS NOTE: ANY OTHER INDICATION REQUIRES MICROBIOLOGY APPROVAL CODE (as for RED ANTIBIOTICS)
Aciclovir IV	1) Use by HLTX, BMT and HIV medical units 2) Use by neurology unit for suspected herpes simplex encephalitis.
Amikacin	Treatment of MAC in HIV patients
Azithromycin PO	Prevention and treatment of MAC in HIV patients
Azithromycin IV	Community-acquired pneumonia (CAP) with Pneumonia Severity Index (PSI) >90*, where oral roxithromycin is inappropriate
Cefepime	1) Serious pseudomonal infection in patients with non-anaphylactic penicillin allergy, in combination with an aminoglycoside 2) Febrile neutropenia, in combination with an aminoglycoside
Ceftriaxone/Cefotaxime	**Ceftriaxone 1g daily or Cefotaxime 1g TDS:** 1) Intra-abdominal bacterial sepsis in patients over 70 years, or with calculated creatinine clearance < 70 mL/min, or with non-anaphylactic penicillin allergy 2) Community-acquired pneumonia (CAP) with Pneumonia Severity Index (PSI) >90* 3) Moderately severe, radiologically proven hospital-acquired pneumonia (HAP), or less severe HAP/CAP in a patient with non-anaphylactic penicillin allergy **Ceftriaxone 2g BD or Cefotaxime 2g QID:** Bacterial meningitis where the organism is unknown or penicillin resistant
Ciprofloxacin IV Ciprofloxacin PO	Only where gentamicin is contraindicated. For serious infection due to a resistant Gram negative organism (eg Pseudomonas) in patients with a contraindication to gentamicin (ie pts over 70 years, or with calculated creatinine clearance < 70 mL/min.) The IV formulation may be used only where oral therapy is inappropriate. Any oral use >5days requires microbiology approval.
Clarithromycin	1) Treatment of MAC in HIV patients 2) Use by gastroenterologists as part of combination *H. pylori* eradication
Fluconazole IV	HIV medicine, HLTX and BMT units for appropriate fungal prophylaxis and treatment, where oral therapy is inappropriate
Itraconazole	HIV medicine, BMT, HTLX units for appropriate fungal prophylaxis and treatment
Piperacillin + Tazobactam (Tazocin®)	1) Severe intra-abdominal sepsis in patients over 70 years, or with calculated creatinine clearance < 70 mL/min 2) Severe hospital-acquired pneumonia (eg. RR>30, PO2 <60, SaO2<90%, SBP<90 mm Hg, or acute renal failure)
Sodium Fusidate	Significant MRSA infection in combination with rifampicin
Ribavirin (SAS)	For proven respiratory syncytial virus (RSV)
Teicoplanin	Significant MRSA infection where the patient is hypersensitive to vancomycin and oral therapy is inappropriate
Terbinafine	**1.** Dermatology use for laboratory-proven dermatophyte infection. **2.** Proven *Scedosporium Prolificans* infections
Ticarcillin +Clavulanate (Timentin®)	1) Febrile neutropenia in combination with an aminoglycoside 2) Serious pseudomonal infection in combination with an aminoglycoside 3) Suspected pseudomonal infection in CF patients post-transplant while awaiting cultures 4) Severe intra-abdominal sepsis in patients over 70 years, or with calculated creatinine clearance < 70 mL/min 5) Severe hospital-acquired pneumonia (eg. RR>30, PO2 <60, SaO2<90%, SBP<90 mm Hg, or acute renal failure)
Valganciclovir	1) CMV retinitis in patients with AIDS 2) Treatment and prophylaxis of CMV in solid organ transplants
Vancomycin IV	1) Febrile neutropenia unresponsive to first line therapy 2) Clinically significant MRSA infection 3) Empiric therapy of line sepsis in patients with MRSA, or at high risk of MRSA, while awaiting cultures
Vancomycin PO	Second line *C. difficile* treatment after failure of a 10 day course of oral metronidazole, or after a second relapse following metronidazole therapy

* To be calculated as per Therapeutic Guidelines - Antibiotic 13th Edition   *9th March 2009*

Appendixes — Resource materials

Government of South Australia

Central Northern Adelaide
Health Service

ROYAL ADELAIDE HOSPITAL - RESTRICTED ANTIBIOTICS DECLARATION FORM

Patient Details (use patient sticker if available)	**Turn over for list of restricted antibiotics and usage guidelines**
Name: _____ Ward: _____ UR No:_____	

Antibiotic	
Dosage Regimen	
Duration	

Please tick boxes / provide details for relevant sections

☐ **EMPIRIC USE**
Infecting organism(s) unknown
- 3 day review of therapy required

OR

☐ **DIRECTED THERAPY**
Infecting organism(s) known
- 7 day review of therapy required
(Please provide details below)

INDICATION

Please tick appropriate box on reverse side. Give details below if indication <u>not</u> listed:

_____

_____

NOTE: Infectious Diseases or Clinical Microbiology approval may be required for other indications

CULTURE AND SENSITIVITY DATA

Organism(s)   _____ _____ _____

Sensitive to   _____ _____ _____

Resistant to   _____ _____ _____

☐ **Recommended infectious disease or clinical microbiology approval**

Details: _____

REQUESTING DOCTOR (print)   _____   **PAGER NO** _____

PHARMACIST (print)   _____   **DATE** _____

Please contact the clinical pharmacist or antibiotic pharmacist if additional assistance is required

ANTIBIOTIC	USAGE GUIDELINES – approved indications, usual dosage regimens

CEFTRIAXONE 1 g injection ($3.95)	☐ **Treatment of:** ( ) lower respiratory tract infections, ( ) urinary tract infections, ( ) cholecystitis, ( ) ascending cholangitis, or ( ) pelvic inflammatory disease, **under the following circumstances:**
	     ☐ In patients hypersensitive to penicillins (excluding immediate hypersensitivity) ***OR***
	     ☐ Due to susceptible organisms (resistant to earlier generations of cephalosporins) ***OR***
	     ☐ Where the use of aminoglycosides are contraindicated due a calculated creatinine clearance of ≤20mL/min or evidence of accumulation as per SEBA-Gen
	 ☐ Empirical treatment, with penicillin, of bacterial meningitis pending culture and sensitivity results
	 ☐ Acute epiglottitis, orbital / periorbital cellulitis, and gonococcal infections
	 ☐ Prophylaxis for meningococcal contacts
	 ☐ Spontaneous bacterial peritonitis pending culture and sensitivity results

CIPROFLOXACIN **oral** only ☐ 500 mg tablet ($0.99) ☐ 750 mg tablet ($1.39)	☐ Infections due to *Pseudomonas aeruginosa* or other Gram negative bacteria resistant to all other oral agents ☐ Bacterial gastroenteritis in severely immunocompromised patients ☐ Bone and joint infections, epididymo-orchitis, prostatitis or perichondritis of the pinna, involving proven/ suspected Gram negative or Gram positive bacteria resistant to all other appropriate agents • Usual dose: 500 – 750 mg twice daily
FAMCICLOVIR 250 mg tablet ($1.07)	**See RAH Antiviral Guidelines for dosage recommendations** ☐ Mucocutaneous herpes (herpetic whitlow, eczema herpeticum) ☐ Genital herpes – initial, episodic or suppression of recurrent infection ☐ Herpetic blepharitis, with aciclovir eye ointment (Ophthalmology consult recommended) ☐ Herpes zoster (shingles) – initial infection in all patients (within 72hrs of rash onset) ☐ Zoster ophthalmicus (Ophthalmology consult recommended) ☐ Varicella (chicken pox) – complicated cases or immunocompromised patient
FLUCONAZOLE ☐ 100 mg cap ($1.97) ☐ 200 mg cap ($3.40) ☐ 200 mg injection ($22)	☐ Oropharyngeal / oesophageal candidiasis ☐ Serious candida infections in patients unable to tolerate amphotericin B • Usual dose: 200 – 400 mg once daily
ITRACONAZOLE ☐ 10 mg/mL solution ($146 for 150 mL) ☐ 100 mg capsule ($2.89)	☐ Treatment/ prophylaxis of systemic candidiasis (not responding to other agents), aspergillosis histoplasmosis, cryptococcosis in immunocompromised patients intolerant of or not responding to amphotericin B ☐ Long term suppression of above infections after amphotericin B treatment • Treatment: 200 – 400 mg once daily • Prophylaxis or suppression:100 – 200 mg once daily • Specify oral solution for high risk patients or when high blood levels required
PIPERACILLIN 4 g injection ($25.71)	☐ Treatment of *Pseudomonas aeruginosa* infections in combination with another anti-pseudomonal agent • Usual dose: 4 g every 8 hours
TOBRAMYCIN 80 mg injection ($2.14)	**See RAH Aminoglycoside Guidelines for dosing and monitoring** ☐ Treatment of *Pseudomonas aeruginosa* infections, in combination with another anti-pseudomonal agent, **and** where there is proven resistance to gentamicin • Usual dose: 5 – 7 mg/kg as first dose, adjusted based on serum levels and renal function

RAH Pharmacy Department, August 2005, revised November 2006, July 2007, October 2008

Government of South Australia

Central Northern Adelaide
Health Service

ROYAL ADELAIDE HOSPITAL

Guidelines for the Management of Hospital Acquired Pneumonia

Not for immunosuppressed or ventilated patients

Definition: pneumonia that is not incubating upon admission, and differs in causative micro-organisms from community acquired pneumonia. In general, patients developing pneumonia (as defined in Therapeutic guidelines, Antibiotic) after 48 hours of admission qualify as hospital acquired (nosocomial) infections.

Initial Investigations:
- Urgent CXR, electrolyte, urea, creatinine, glucose, LFTs, CBE & differential, SaO_2, and arterial blood gas (if $SaO_2 < 94\%$)
- **Prior to the initiation of antibiotic therapy, specimens should be sent for identification of causative organism.**
    - o Blood cultures
    - o Sputum Gram stain and culture including Legionella
    - o Nasopharyngeal aspirate/swab in viral transport medium or sputum for rapid viral detection
- The following specimens should also be obtained
    - o Urinary Legionella antigen detection

Mild to Moderate
amoxycillin + clavulanic acid 875/125 mg (1 tablet) orally 12 hourly

Or

cephazolin 1 g IV 8 hourly **plus** Gentamicin* 5 mg/kg/day IV
Due to risks of ototoxicity and nephrotoxicity, it is recommended that gentamicin should be **ceased** after 3 days unless strongly indicated

If CrCl < 30 mL/min use ceftriaxone 1 g IV daily

Add metronidazole 500 mg IV 12 hourly if suspect aspiration or recent thoraco-abdominal surgery

For patients with a history of anaphylaxis to penicillin and/or who have an allergy to cephalosporins consult Infectious Diseases or Clinical Microbiology

Alternative therapy needs discussion with Infectious Diseases or Clinical Microbiology

Response to treatment should be assessed at 48-72 hours after initiation of therapy

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Severe
Seek advice from Infectious Diseases or Clinical Microbiology in all cases

Preferred regimen piperacillin/tazobactam (Tazocin®) 4.5 g IV 8 hourly **plus** Gentamicin* 5 mg/kg/day IV

(Piperacillin/tazobactam (Tazocin®) requires approval from Infectious Diseases or Clinical Microbiology)

In patients known to be colonised with, or at high risk of MRSA, vancomycin should be added.

*Consult the once daily aminoglycoside chart for dosing and monitoring.

Approved by the Antibiotic Working Party of the RAH Drug Committee September 2005, December 2005, May 2009

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HUNTER NEW ENGLAND HEALTH

Facility_____

EMERGENCY DEPARTMENT ADULT COMMUNITY ACQUIRED PNEUMONIA MANAGEMENT

JHH7F

Signs/Symptoms	Score ONE point for each feature present
Confusion New onset or worsening of existing state if cognitive impairment present	
Oxygen Rate PaO$_2$ <60mm Or O$_2$ sat < 90%	
Respiratory Rate ≥30/min	
Blood Pressure systolic BP <90mmHg or diastolic ≤ 60mmHg	
Total Score	

Empiric Antibiotic Therapy	MILD score = 0	MODERATE score = 1	SEVER/ICU/HDU[1] score = 2 or more
First line	amoxycillin 500mg tds oral	penicillin G 1.2g q6h IV After inpatient team review +/- Doxycycline	penicillin G 1.2g q4h IV AND gentamicin[2] 5mg/kg daily IV AND azithromycin 10mg/kg up to 500mg/day IV (max 5d usual)
Penicillin allergy	doxycycline 200mg stat, then 100mg daily	doxycycline 200mg stat, then 100mg daily	ceftriaxone 1g daily IV AND azithromycin 10mg/kg up to 500mg/day IV (max5d usual)
Notes	***MRSA pneumonia has high mortality: always consult Infectious Diseases***	[1] Add vancomycin if staph pneumonia possible: 1g IV 12-hourly (max infusion 1g/h). Target trough=10-20mg/ [2] Gentamicin dose is based on calculated 'ideal' body wt. Avoid gentamicin if hearing/vestibular problems.	
Investigations In ED	FBC, U/E/C, Blood culture, Store serum (virology), BSL	**Add:...** LFTs, Blood cuiture (2 sets), Mycoplasma IgM (acute serum), Sputum micro/culture, Severe: add Legionella culture and urine LP antigen, viral throat/nose swabs (influenza PCR and extended respiratory virus pcr)	
	Likely suitable for home treatment Social Supports No unstable co-morbidities	**Hospital Admission** Consider ICU Consultation (2 or more CORB factors or respiratory failure)	
	All immunocompromised patients: seek consultant advice		

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Doctor Name (print) _____ Doctor Name (Signature) _____

Date: _____ Time: _____

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EMERGENCY DEPARTMENT ADUL COMMUNITYT ACQUIRED PNEUMONIA MANAGEMENT

Emergency

Community-Acquired Pneumonia (CAP) Guidelines for Adults

A synopsis of this guideline is available as a laminated ID-sized card from your hospital pharmacy.

Key Points:

Correct identification of severe pneumonia enables appropriate investigation, early broad spectrum antibiotic therapy (that includes Legionella cover) and necessary respiratory support.

Time to Antibiotic: One of the PhD (Maggie) project key performance indicators is the time taken from MO review until first antibiotic administered. Antibotic administration within 4 hours of arrival is associated with decreased mortality and length of stay.[1]

***Streptococcus* pneumoniae remains the most important cause of CAP in our community.**
Amoxycillin and penicillin G retain efficacy in CAP due to pneumococcal strains with raised MICs to betalactams. Penicillin-G is also active against most (80%) of *Haemophilus influenzae.*

Serology testing: Acute serum sent for Mycoplasma Igm will be stored by Virology for later testing. Testing for other causes will proceed once a convalescent sample (at least 3 weeks after on set) is received with a pathology request.

PCR diagnosis strategy for respiratory viruses: The combined nose/throat sample for flu PCR has a special collection procedure (see below). Extended respiratory virus PCR currently should be requested on all Severe CAP cases.

Atypical pathogens: Legionella diagnosis has important public health implications. Please do not neglect the additional tests for legionella, particularly if renal failure and/or GI symptoms present.
If atypical pneumonia is suspected, seek consultant advice and consider possible addition of doxcycyline.

Azithromycin is retained for severe CAP in order to provide cover against pertussis and other atypical pathogens.

MRSA strains with enhanced potential for causing pneumonia are circulating in the community. Adult vancomycin dosing recommendations have changed recently. Doses are calculated on total body weight.

Immunocompetency: patients with chronic cardias, respiratory or neurological problems or who are immunocompromised patient with CAP seek consultant advice.

Community Procedure: nasal/throat swab for Influenza PCR

Equipment (Emergency Departments in JHH and Belmont have available a collection kit)
- Viral swabs (green top viral transport swab) x 2 **(must be correct swab type)**
- Normal saline (0.9%) 10mL disposable plastic ampule
- Wooden or plastic disposable tongue depressor
- Personal protective equipment (surgical mask, eye goggles)
- Alcohol hand gel (Aqium)

Procedure
1. Explain the procedure to the patient.
2. Clean hands with alcohol gel (aquim) and put on PPE (protective glasses and mask)
3. Take viral culture **nasal swab**
    - moisten swab with sterile normal saline
    - sample the anterior nostril by gently abrading the nasal mucosa on both sides
    - insert swab into transport medium.
4. Take viral culture **Throat swab**
    - take the other swab and moisten in sterile normal saline
    - sample both tonsils and the posterior oropharynx with the swab. Avoid touching the swab on the tongue or other parts of the mouth.
    - insert swab into transport medium
5. Forward the labelled specimens to HAPS ASAP
6. Discard PPE and **clean hands with alcohol gel** or hand wash.

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[1] Houck PM, et al Administration of first hospital antibiotics for community-acquired pneumonia: Curr Opin Infect Dis 2005:18:151-156

CLINICAL PRACTICE GUIDELINE	HUNTER NEW ENGLAND NSW⊕HEALTH

Community-Acquired Pneumonia (CAP) Guidelines for Adults and Children

Document Registration Number: HNEH CPG 09_06

Sites where CPG applies	Acute Networks Hospitals
	Primary & Community Networks
Target Clinical Audience	This CPG is applicable to adults and children (all age groups other than neonates).
	All clinicians who treat community-acquired pneumonia
	Pharmacists
Applicability	*(Please indicate with a X in the appropriate box)*
*NB: *Please be aware that young people between 16 and 18 years of age may have a number of other guideline, policy or legal requirements that should be adhered to but for the purposes of guideline development can be considered adult	Neonate – less than 29 days ☐
	Children up to 16 years* Y
	Adult (18 years and over) Y
	All of the above ☐
Summary	This document describes expert recommendations relating to management of CAP in facilities managed by Hunter New England Health Service.
Keywords	Pneumonia, *Legionella*, influenza antibiotic stewardship
Replaces existing clinical practice guideline or policy?	Yes
Registration Numbers of Superseded Documents	HNEH CPG 08_03

Related documents (Policies, Australian Standards, Codes of Conduct, legislation etc)

Detail main parent documents that informs this CPG

- Therapeutic Guidelines: Antibiotic, Therapeutic Guidelines, Melbourne, Victoria 2006
- Buising, K et al. Identifying severe community-acquired pneumonia in the emergency department: A simple clinical prediction tool. Emergency Medicine Australasia (2007) 19, 418–426

Clinical Network/stream leader responsible for CPG

Contact Person/Position Responsible
Contact Details

Review Due Date:	July 2012
Date authorised by Area Quality Use of medicines	14 April 2009
Date authorised by Area Clinical Network/stream	March 2009
Date Authorised by HNE Clinical Quality and Patient Safety Committee	29 July 2009
Trim Number	09/101-1-6

Version One   July 2009

Appendixes — Resource materials

CLINICAL PRACTICE GUIDELINE	HUNTER NEW ENGLAND NSW⊕HEALTH

Community-Acquired Pneumonia (CAP) Guidelines for Adults and Children

1.0   Glossary

AFB	acid fast bacilli – e.g. *Mycobacteria* species such as tuberculosis
BAL	Broncho-alveolar lavage
CAP	community-acquired pneumonia
CAPAC	Community Acute Post-Acute Care (CAPAC)- hospital in the home care team that operates from several HNE Centres
CI	Contraindication
CORB	acronym for the severity scoring system (**C**onfusion, **O**xygenation, **R**espiratory rate, **B**lood pressure) in use for CAP assessment in adults
HAP	Healthcare (hospital)-associated pneumonia
HAPS	Hunter Area Pathology Service
HDU	High Dependency Unit
ICU	Intensive Care Unit
IV	Intravenous
LP1	*Legionella pneumophila* serogroup 1, the commonest cause of legionellosis
MRSA	methicillin-resistant *Staphylococcus aureus*
NPA	nasopharyngeal aspirate
P2 mask	particulate filter mask used for protection against airborne fine particle infected aerosols
PCR	Polymerase chain reaction – a test that amplifies very small quantities of DNA or RNA from a pathogen within a sample so that detection (diagnosis) can occur
PPE	personal protective equipment (e.g. mask, gown, gloves, eye protection)
RSV	Respiratory syncytial virus – the commonest cause of bronchiolitis in infants. Also a cause of pneumonia in adults

2.0   GUIDELINE

Executive Summary

Correct management of community-acquired pneumonia (CAP) improves patient outcomes. Important aspects of management include:

- Clinical assessment to identify unusual risk exposures
- Severity assessment using the CORB (**C**onfusion, **O**xygenation, **R**espiratory rate, **B**lood pressure) scoring at presentation (use the worst parameters recorded for each during the ED stay or first 24 hrs) to identify patients with severe pneumonia. CORB can also be used to assess patients with influenza-like illness.
- Investigation of patients with severe pneumonia to demonstrate an infective cause that enables later targeting of antibiotic therapy
- Influenza testing of admitted CAP cases during May-November period. Pending influenza results, start antiviral treatment for patients with recent onset of symptoms (< 72hrs) or with severe disease (at any time following symptom onset)
- Broad spectrum empiric antibiotic treatment for all severe cases to ensure that atypical causes such as *Legionella* and Gram negative pneumonia are treated from the outset.
- Cases of severe pneumonia due to strains of community MRSA are becoming more frequent in Northern NSW. It is important to give consideration to this diagnosis and adjust empiric treatment if pneumonia due to *Staph. aureus* is considered possible.

A synopsis of this guideline is available as a laminated ID-sized card from your hospital pharmacy service.

Clinical Assessment (adults)

*In view of the danger to healthcare staff posed by transmissible respiratory pathogens such as influenza, it is essential that **Droplet Additional Infection Control Precautions** are followed (alcohol hand rub, don personal protective equipment upon room entry- surgical mask and protective eye wear) for all clinical interactions and specimen collection. Collection of NPA requires donning of P2 mask, protective eye wear, long sleeve impervious gown and gloves in that order- seek advice if uncertain about this PPE process.*

Mild pneumonia

- Social supports; **AND**
- No unstable comorbidities; **AND**
- Non-severe CAP by clinical and diagnostic criteria below.

Moderate pneumonia

- Non-severe cases requiring admission (see admission criteria below).

Severe pneumonia (CORB criteria)- 2 or more of:

- **Confusion**   new onset or worsening of existing state if cognitive impairment present
- **Oxygen** PaO_2 <60mm Or O_2 sat $\leq$ 90%
- **Respiratory Rate** $\geq$ 30/min
- **Blood Pressure**   systolic BP <90mmHg or diastolic $\leq$ 60mmHg

Is it 'severe' pneumonia?

This is the most important determination. Presence of two or more CORB criteria is sufficient to indicate presumptive severe pneumonia (quite aside from whether the patient has or will be admitted to ICU) and indicates that broad-spectrum empiric antibiotics are required from the start. The therapy is selected to particularly provide adequate cover for:

- *Streptococcus pneumoniae* (i.e. benzylpenicillin)
- *Legionella* (azithromycin)
- aerobic Gram negatives such as *Klebsiella* species (gentamicin)
- *Staph. aureus* (gentamicin or add vancomycin to cover community methicillin-resistant *Staph. aureus* (MRSA) if suspicion high- see Sputum examination below).

An assessment of the patient by the ICU team is advisable in all severe cases.

For assessment of children, consult the Clinical Pathway at the back of this document

Admission Criteria

Patients who have no preceding cardiac and respiratory disease and who present with mild pneumonia can usually be managed as an outpatient. ***All of these patients need review the next day by their General Practitioner (GP) or the Community Acute Post-Acute Care (CAPAC) team and later review by their GP.***

Patients with chronic cardiac, respiratory or neurological problems or who are immuno-suppressed, are at higher risk of complications and should be considered for admission. All immunocompromised patients with CAP should be discussed with a consultant before discharge.

Patients who have failed to respond to a reasonable course of oral antibiotics, should be considered for admission and parenteral therapy. Clinical judgement and the patient's social circumstances are important factors in this decision.

Appendixes — Resource materials

Diagnostic considerations

Relevant considerations include:
- Season (winter- pneumococcus, Respiratory syncytial virus (RSV) (even in adults; onset of season often in May), Influenza (June to November usually)
- Comorbid conditions Chronic Airflow Limitation (*Haemophilus*), other lung disease (complex)
- exposure to birds (psittacosis), potting mix or gardening (*Legionella longbeachae*), animals/rural (*Coxiella burnetii* - Q Fever)
- pregnancy- throughout pregnancy and puerperum, women are at risk from severe influenza

The clinical and radiological presentation seldom permits prediction of the aetiology. Occurrence of abscess(es) indicates a pyogenic cause (e.g. *Staph. aureus*, β-haemolytic strains of streptococci, anaerobic organisms, *Klebsiella* species.)

Presence of sudden onset rigors, pleuritic pain, purulent sputum with lobar consolidation has a sensitivity of 30% and specificity of 91% for pneumococcal pneumonia.

Presence of an asthma-like presentation in adult with prominent wheeze is suggestive of primary RSV pneumonia.

Recommended Laboratory Investigations

Routine
All patients in the Emergency Department (ED) :
- Two blood culture sets (20mLs in two bottles for adult/adolescent, 3-5mLs in child in to single bottle). Collect with correct asepsis from different venepuncture sites. Collect prior to antibiotics.

Additional Investigations for Patients Requiring Admission
In the ED:
- Serum for *Mycoplasma* IgM (acute-phase).
- Sputum microscopy and culture.

In the ED or on the ward:
- Naso-pharyngeal aspirate (NPA) for respiratory virus testing and bacterial culture (infants < 2yr only).
- May to November- Influenza PCR on nose and throat swab sample (NPA is an acceptable alternative from infants).
- Consider urine for *Legionella* LP1 antigen.

Additional Investigations for Patients with Severe CAP (see Appendix A- Checklist for Severe CAP in ICU)

- Sputum *Legionella* culture and PCR.
- Urine for *Legionella* (LP1) and *Streptococcus pneumoniae* antigens (can be collected up to 1 week post presentation).
- NPA or BAL for extended respiratory virus detection (in ICU), especially if initial influenza testing is negative.

Notes on investigations:

Legionella detection
Detection is by culture and polymerase chain reaction (PCR) nucleic acid detection (must be specifically requested from HAPS) AND urinary antigen detection for *Legionella pneumophila* serogroup 1 antigen. See also Acute Serology, next section below.

Sputum gram stain and culture
If the patient can produce a well-expectorated specimen (not salivary), presence of typical organisms suggestive of either *Strep. pneumoniae* (pneumococcus -Gram positive diplococci) or *Haemophilus* (small Gram negative rods) had the following sensitivity and specificity in one of many studies:

	S. pneumoniae (presumptive)	*Haemophilus* (presumptive)
Sensitivity	56%	82%
Specificity	97%	99%

Presence of predominant Gram positive cocci in clusters, i.e. Staphylococci and profuse white cells indicates probable *Staph. aureus* pneumonia. In this case pre-treatment blood cultures are often positive within 24hrs.

Acute Serology
Acute serum for *Mycoplasma* IgM is usually tested twice a week in the laboratory. For other causes, an acute serum is important but it may be held untested (as it would normally be negative) until a convalescent serum is also received in the laboratory (at least 3 weeks after onset of illness). Note that delayed seroconversion is the rule in L*egionella* infection. If *L. longbeachae* is suspected, then request this specifically as routine *Legionella* serology seldom picks this up.

Mycobacterial Ziehl-Nielsen (acid fast bacilli- AFB) stain and culture
Should be considered in the appropriate clinical circumstance, and is a particular concern in the elderly, immunosuppressed and immigrants from high prevalence countries.

Pleural fluid studies
Presence of significant amount of pleural fluid should prompt aspiration for microscopy, biochemistry and culture (+/- AFB examination). The presence of a complicated parapneumonic effusion dictates urgent drainage. Where TB is a possibility, pleural biopsy with culture is optimal for detection.

Viral detection
Nasopharyngeal aspirate or bronchial lavage/washing best in infant or ICU case. Testing will usually be by PCR for an extended range of respiratory viruses (sent away); if rapid immunofluorescence testing required, then this must be specifically requested.

Combined nose/throat swab during influenza season- request Influenza PCR.

Initial ICU experience in 2009 shows that repeat influenza testing from a nasopharyngeal aspirate or lower tract sample is of value in confirming a diagnosis in patients with initial negative results from nose/throat.

Empiric antimicrobial therapy in the non-immunocompromised host
Empiric therapy should be carefully reviewed and substituted with directed (targeted) therapy against a demonstrated pathogen as soon as possible. In particular it may be possible to cease gentamicin or switch to an oral option. See Therapeutic Guidelines: Antibiotic for specific targeted recommendations.

The usual duration of antimicrobial therapy for non-severe CAP is 3-7 days. Early cessation is recommended if viral pneumonia is proven.

NB*. During the influenza season, all admitted cases of CAP with recent onset of symptoms (< 72hrs) should also be considered for oral oseltamivir treatment after collection of influenza investigations (nose/throat swab usually). In confirmed cases, continue anti-viral treatment for 5 days and consider cessation of antimicrobials. ICU patients may need longer treatment.*

	Mild	Moderate	Severe/ICU/HDU[1]
First line	Amoxycillin 15mg/kg up to 500mg tds oral	Benzylpenicillin 30mg/kg up to 1.2g q6h IV After inpatient team review oral doxycycline may be added dependent on assessment and previous treatment details.	Benzylpenicillin 30mg/kg up to 1.2g q4h IV **AND** Gentamicin[2] 5mg/kg (ideal weight) daily IV **AND** Azithromycin[3] 10mg/kg up to 500mg /d IV
Penicillin allergy or gentamicin CI[2]	Adult or older child: Doxycycline 200mg stat, then 100mg daily oral Child under 9yrs: Roxithromycin 4mg/kg up to 150mg q12h oral		Ceftriaxone 25mg/kg up to 1g daily IV **AND** Azithromycin 10mg/kg up to 500mg/d IV
Immediate β-lactam allergy	Same		Vancomycin 25mg/kg up to 1g IV 12-hrly **AND** Gentamicin[2] 5mg/kg (ideal weight) daily IV **AND** Azithromycin 10mg/kg up to 500mg/d IV

Notes

[1.] **Add IV vancomycin if *Staph. aureus* pneumonia possible**: 25mg/kg up to 1g IV 12-hrly Use actual body weight. Change to flucloxacillin if methicillin-susceptible. Continue vancomycin if MRSA proven. Adjust doses to achieve trough levels of 10-20mg/L. MRSA pneumonia has high mortality: always consult Infectious Diseases.

[2.] **Contraindications (CI) for use of aminoglycosides include:**
- pre-existing significant conductive hearing loss or vestibular problems including - dizziness, vertigo or tinnitus
- previous vestibular or auditory toxicity due to an aminoglycoside or serious hypersensitivity to an aminoglycoside (rare)
- relative CI- cholestasis (bilirubin > 90uM/L)- increased risk of drug-induced renal failure

Patients with chronic renal failure or deteriorating renal function can safely be given empiric doses of gentamicin provided there are no other contraindications. Also see **HNE CPG Aminoglycosides dosage and monitoring (adult).**

Dose of gentamicin in obese patients is based on ideal body weight (IBW):
IBW (**male**)   = 50kg + 0.9kg x [each cm in height over 152cm]
IBW (**female**) = 45kg + 0.9kg x [each cm in height over 152cm]

[3.] **IV azithromycin** should be given as an appropriately diluted infusion over greater than or equal to 60 minutes. It may be given through a peripheral line. Empiric use should usually be ceased at 3 days unless a specific atypical pathogen such as *Mycoplasma* or *Legionella* has been demonstrated. Early switch to oral azithromycin is worthwhile. Note that *Coxiella burnetii* (Q-Fever agent) is NOT susceptible to azithromycin- use doxycycline instead.

Possible causes of treatment failure

Reason for failure	Examples
Incorrect diagnosis	pulmonary embolism, pulmonary oedema, pulmonary eosinophilia, Wegener's granulomatosis, drug allergy, lung cancer
Resistant organism/infection	*Mycoplasma pneumoniae, Chlamydia psittaci, Coxiella burnetii, Staphylococcus aureus*, β-lactamase-producing *Haemophilus influenzae (unusual)* viral infection unrecognised pulmonary tuberculosis *Pneumocystis carinii*
Inadequate drug, dose or route of administration	oral erythromycin for *Legionella* infection azithromycin for *Coxiella burnetii (Q Fever)*
Complication	empyaema, abscess, pulmonary embolism, fever related to drug therapy
Underlying disease	lung cancer, cardiac failure, immunodeficiency

Community-acquired pneumonia treatment pathways

The adult CAP pathway (see overleaf) incorporating the CORB severity scoring system was implemented across HNE Emergency Departments in 2008. Pathway is produced overleaf and is available on SALMAT.

A separate paediatric version is also available (overleaf)

The CAP/HAP business card-sized summary is available from Acute Networks Pharmacy Departments. An image of the text is opposite.

Community Acquired Pneumonia

Criterion	First line	Pen.allergy
Mild Social supports OK Stable comorbidities No CORB factor(s)	amoxycillin 15mg/kg up to 500mg tds oral	Child under 9yrs: **roxithromycin** 4mg/kg up to 150mg q12h Others: **doxycycline** 200mg stat, then 100mg/d
Moderate 1 or less CORB factors OR Requires admission for another reason *(may still require ICU assessment)*	benzylpen 30mg/kg up to 1.2g q6h IV **+/-doxycycline** (age >8 yrs) if atypical cover required	
Severe/ICU/HDU[1] Adult with ≥ 2 of: **C**onfusion: new onset pO_2<60mm or O_2sat≤90% **R**R ≥30/min **B**P- (sys. <90mmHg or diast. ≤60mm Hg)	benzylpen 30mg/kg up to 1.2g q4h IV **AND** **gentamicin** 5mg/kg daily IV **AND** **azithromycin** 10mg/kg up to 500mg/day IV (max 5d usual)	ceftriaxone[2] 25mg/kg up to 1g daily IV **AND** **azithromycin** 10mg/kg up to 500mg/d IV (**stop at 3 days** if no atypical pathogen demonstrated)

Invest. (severe): blood-cult. sets x2, *Mycoplasma* IgM, **urine**- *Legionella* & pneumo. antigen, **nose/throat**-'flu PCR, **NPA**-resp. virus det., **sputum**–m/c/s & *Legionella* cult./PCR

Notes: [1]Add vancomycin if staph pneumonia possible: **25mg/kg up to 1 gram IV 12-hrly** (max. rate 1g/hr). Use actual body weight. Target trough is 10-20mg/L. **Consult ID**.
[2]For immediate hypersensitivity, use **vancomycin, gentamicin, azithromycin**

Expires Dec 2010

Appendixes — Resource materials

HUNTER NEW ENGLAND AREA HEALTH SERVICE

Facility _____

EMERGENCY DEPARTMENT ADULT COMMUNITY ACQUIRED PNEUMONIA MANAGEMENT

PLEASE USE GUMMED LABEL IF AVAILABLE

SURNAME		UNIT NUMBER
OTHER NAMES		
ADDRESS		
DOB	M.O.	
HOSPITAL / WARD		

Signs/Symptoms	Score ONE point for each sign/symptom present
Confusion New onset or worsening of existing state if cognitive impairment present	
Oxygen Rate PaO₂ <60mm Or O₂ sat ≤90%	
Respiratory Rate ≥30/min	
Blood Pressure systolic BP <90mmHg or diastolic ≤60mmHg	
Total Score	

Empiric Antibiotic Therapy	MILD score = 0	MODERATE score = 1	SEVERE/ICU/HDU# score = 2 or more
First line	amoxycillin 500mg tds oral	benzylpenicillin 1.2g q6h IV After inpatient team review +/- doxycycline 200mg stat then 100mg daily	benzylpenicillin 1.2g q4h IV AND gentamicin* 5mg/kg daily IV AND azithromycin 10mg/kg up to 500mg/day IV (max 5d usual)
Penicillin allergy	doxycycline 200mg stat, then 100mg daily	doxycycline 200mg stat, then 100mg daily	ceftriaxone 1g daily IV AND azithromycin 10mg/kg up to 500mg/day IV (max5d usual)
Notes	*MRSA pneumonia has high mortality: always consult Infectious Diseases*	**Add** vancomycin if staph pneumonia possible: 1g IV 12-hourly (max infusion 1g/h). Target trough=10-20mg/L * gentamicin dose is based on calculated 'ideal' body wt. Avoid gentamicin if hearing/vestibular problems.	
Investigations in ED	FBC, U/E/C, Blood culture, Store serum (virology), BSL	**Add** LFTs, Blood culture (2 sets), Mycoplasma IgM (acute serum), Sputum micro/culture. Severe: add Legionella culture/PCR and urine LP antigen, viral throat/nose swabs (influenza PCR and extended respiratory virus PCR).	
	Likely suitable for home treatment Social Supports No unstable co-morbidities	**Hospital Admission** Consider ICU Consultation (a score of 2 or more (CORB factors) or respiratory failure). Significant aspiration pneumonia: add metronidazole IV or oral (refer TG: Antibiotic, Edition 13, page 225).	
	All immunocompromised patients: seek consultant advice		

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Date: _____ Time: _____   Designation _____

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(left text: 08/08 (August 2008))

HUNTER NEW ENGLAND AREA HEALTH SERVICE
EMERGENCY DEPARTMENT

**Paediatric Community Acquired Pneumonia
Management Guidelines
(Age 4 months – 17 years)**

PLEASE USE GUMMED LABEL IF AVAILABLE	UNIT NUMBER
SURNAME	
ADDRESS	
DATE OF BIRTH	M.O.

*This pathway is for suspected viral or bacterial pneumonia in children who are greater than 4 months old. Excluded from this pathway are (patients with <u>any</u> one of these):
- Patients less than 4 months old
- Patients immunocompromised
- Patients with congenital heart disease
- Patients with Cystic Fibrosis
- Patients with effusion
- Patients with pneumatoceles

*If bronchiolitis considered please use appropriate pathway.
For the above exclusions early consultation with a Paediatric Respiratory Specialist should be undertaken once initial stabilisation has occurred.

Features of viral lower respiratory tract infection	Features of bacterial lower respiratory tract infection	Features of *Mycoplasma* lower respiratory tract infection
▪ Cough ▪ Infants and young children ▪ Wheeze ▪ Fever < 38.5 °C ▪ Marked recession ▪ Hyperinflation ▪ CXR shows hyperinflation and patchy change ▪ Lobar collapse when severe	▪ Cough ▪ Fever > 38.5 °C ▪ Respiratory rate> 50 ▪ Chest recession ▪ Wheeze not a sign (other than *Mycoplasma*) ▪ Clinical and CXR signs of consolidation rather than collapse	▪ Cough ▪ School children ▪ Wheeze, crackles ▪ Interstitial infiltrates, hilar adenopathy, lobar consolidation ▪ Arthralgia

<u>#Only need to meet one criteria to be assigned to that severity grade (vomiting and temperature excluded)</u>

#Severity Assessment	Mild If all the following criteria are met patient may be discharged from ED *(temperature excluded)*	Moderate *(Hospital Admission)*	Severe *Senior doctor review* *(Requires ICU Admission)*
Temperature	< 38.5 °C	> 38.5 °C	> 38.5 °C
Respiratory Rate	Within normal range for age (see nursing observation sheet for normal range)	Above range given for age (see nursing observation sheet for normal range)	Continuing to rise, and or evidence of exhaustion
Saturation	> 94% in room air	< 94% in room air	Failing to maintain SpO^2 >94% on 6 L FiO^2
Work of breathing (nasal flare, recession)	Mild	Moderate	Severe, may exhibit paradoxical chest wall movement in older child
Vomiting	No	May be present	May be present
Perfusion	No tachycardia	Tachycardia	Shock
Multi-lobar consolidation	No (if diagnosis can be made on history or examination alone – chest x-ray not needed)	No	Yes
Social situation	Family able to provide appropriate observations or supervisions	Family unable to provide appropriate observations or supervisions	N/A

XXX Emergency

PAEDIATRIC COMMUNITY ACQUIRED PNEUMONIA

Emergency XXX

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Appendixes — Resource materials

HUNTER NEW ENGLAND AREA HEALTH SERVICE
EMERGENCY DEPARTMENT

Paediatric Community Acquired Pneumonia
Management Guidelines
(Age 4 months – 17 years)

PLEASE USE GUMMED LABEL IF AVAILABLE		UNIT NUMBER
SURNAME		
ADDRESS		
DATE OF BIRTH	M.O.	

Investigations/Monitoring	Mild	Moderate	Severe
Saturation	YES	YES	YES *(continuous)*
CXR	Consider (see below) *	YES	YES
FBC	NO	YES	YES
UEC	NO	YES	YES
Serology (hold serum)	NO	YES	YES
Blood culture	NO	YES	YES
NPA (RSV)	NO	Discuss with inpatient team	YES
NPA (extended screen)	NO	NO	YES
Flu pCR nose/throat	NO	NO	YES
ABG/VBG	NO	NO	YES

- *Mild CAP - if Diagnosis can be made on history or exam alone then CXR is not needed*
  - *If viral pneumonia withhold antibiotics*

Treatment	Mild	Moderate	Severe
Oxygen	NO	YES	YES
IV fluids, NBM (2/3 maintenance)	NO	YES	YES
Antipyretics Analgesics	YES	YES	YES
Antibiotics (first line)	▪ Amoxycillin 25 mg/kg up to 500 mg TDS oral for 3-5 days	▪ Benzylpenicillin 30 mg/kg up to 1.2g 6 hrly IV for 3-5 days *After inpatient team review may add* ▪ Doxycycline oral 200 mg stat then 100 mg daily if >9 yrs	A. Benzylpenicillin 30 mg/kg up to 1.2 g 4 hrly IV *AND* B. Gentamicin 5 mg/kg IV *AND* C. Azithromycin 10 mg/kg up to 500 mg/day IV (max 5 days)
Antibiotics (penicillin allergy)	Children < 9yrs ▪ Roxithromycin 4 mg/kg up to 150 mg 12 hrly oral for 3-5 days Children > 9yrs ▪ Doxycycline 200 mg stat then 100 mg daily for 3-5 days	Children < 9yrs ▪ Roxithromycin 4 mg/kg up to 150 mg 12 hrly oral for 3-5 days Children > 9yrs ▪ Doxycycline oral 200 mg stat then 100 mg daily for 3-5 days	A. Ceftriaxone 25 mg/kg up to 1 g daily IV *AND* B. Azithromycin 10 mg/kg up to 500 mg/day IV (max 5 days)
Antibiotics (if *Mycoplasma* considered)	▪ Roxithromycin 4 mg/kg up to 150 mg oral 12 hrly for 3-5 days OR ▪ Erythromycin ethyl succinate (EES) 10 mg/kg QID for 3- 5 days	▪ Roxithromycin 4 mg/kg up to 150 mg oral 12 hrly for 5 days OR ▪ Erythromycin ethyl succinate (EES) 10 mg/kg QID for 3-5 days	As above
Disposition	A. Home - GP followup in 2-3 days B. Follow up CXR only if after lobar collapse, an apparent round pneumonia, or continuing symptoms. C. Parent fact sheet	Admit to Ward	Admit to ICU/HDU

Doctor Name (print): _____ Signature: _____ Date __/__/__ Time: _____

3.0 IMPLEMENTATION PLAN

Detail how the clinical practice guideline will be implemented including education and communication strategies ensuring staff knowledge.
It should clearly address WHAT, HOW, WHEN, WHY and WHO statements.

The Chair of the Antimicrobial Working Party will be responsible for the following rollout over the next 1 month:
1. Publicity about the revised CPG to go to JMOs, Registrars, ED, Respiratory Medicine, Infectious Diseases, Divisions of Medicine and Intensive Care streams
2. Issue of small revised CPG card to members of these Streams
3. All EDs to carry the Paediatric and Adult Pathway forms
4. Checklist for ICU investigation to be promoted over the weekly ICU liaison process when individual cases of pneumonia are discussed with Infectious Diseases and Microbiology
5. Infectious Matters Newsletter item in next Edition – goes out to all clinical staff.

4.0 EVALUATION PLAN

Provide evidence that the clinical practice guideline will be evaluated according to clinical effectiveness, socioeconomic impact, compliance and staff acceptance.
It should clearly address WHAT, HOW, WHEN, WHY and WHO statements.

1. Individual patient review takes place during the weekly and twice weekly ICU liaison meetings conducted by Clinical Microbiology. Compliance with the CPG is promoted during these meetings
2. Annual Drug usage evaluation studies of CAP take place at Belmont, JHH and Mater sites with feedback to clinical groups. These DUE studies provide evidence of pathway compliance.

5.0 REFERENCES

Therapeutic Guidelines: Antibiotic, Therapeutic Guidelines, Melbourne, Victoria 2006

Buising, K et al. Identifying severe community-acquired pneumonia in the emergency department: A simple clinical prediction tool. Emergency Medicine Australasia (2007) 19, 418–426

6.0 CONSULTATION LIST

- Infectious Diseases and Immunology, HAPS Microbiology
- Intensive Care and Emergency Departments
- Respiratory Medicine, JHH
- Kaleidoscope network- B Whitehead, M Lee, P Davidson
- Area Quality Use of Medicines Committee
- Anti-microbial Working Group

Appendix A

Investigation Checklist for Severe Community Acquired Pneumonia Cases Admitted to Intensive Care Units

Date collected	Investigation
	Pre-treatment blood cultures – at least two sets (20mLs each set for adult, 3-5mL for child/infant)
	Serum for *Mycoplasma* IgM - this sera automatically is stored as well for later testing
	EDTA blood for *Coxiella burnetti* (Q fever) PCR (adults)
	Throat and nose viral swabs for influenza PCR (May-Nov only)
	Pre-treatment sputum for routine culture and *Legionella* culture & PCR (adults only)
	Urine for *Streptococcus pneumoniae* and *Legionella pneumophila* antigen detection
	NPA/BAL for respiratory virus detection **(send if initial influenza PCR and bacterial cultures are negative at 24hrs)**

Notes:
- Sputum sample is also suitable for *Legionella* culture/PCR and respiratory virus detection.
- Initial ICU experience in 2009 shows that repeat influenza testing from a lower tract sample is of value in confirming a diagnosis in patients with initial negative results from nose/throat.
- Tests as above must be requested specifically on pathology request form. Additional serological requests can be made on sera held in the laboratory by referring back to the relevant lab number.

Guidelines for RGH surgical antibiotic prophylaxis in antibiotic naïve patient

Administration of prophylactic antibiotics, time-frame – aim for no greater than one hour prior to procedure
**NOTE: PROCEDURE = skin incision or application of tourniquet, whichever occurs earlier

Vascular Surgery	Orthopaedic Surgery	Urological surgery	General & Plastic Surgery
VASCULAR RECONSTRUCTION: - AAA repair - Graft / Stent insertion - Carotid endarterectomy *CEPHAZOLIN prior to incision* *if in theatre at 6 hours, repeat 1gm* **RE-DO GRAFTS:** *CEPHAZOLIN and GENTAMICIN,* *repeat CEPHAZOLIN if in theatre after 6 hours* **MRSA +ve:** *VANCOMYCIN 1gm prior to incision* **RECONSTRUCTION IN PRESENCE OF ULCER OR GANGRENE:** *Adjust protocol according to swab results (if no swab results, manage as re-do graft)* **AMPUTATION:** (major or minor) *CEPHAZOLIN plus* *METRONIDAZOLE prior to incision* **AV FISTULA:** *CEPHAZOLIN prior to incision* **OTHER PROCEDURES:** - Thoracoscopic sympathectomy - Varicose vein surgery *Prophylaxis not recommended*	**SURGERY INVOLVING JOINT PROSTHESES** **STANDARD REGIMEN:** *CEPHAZOLIN before skin incision or before inflation of tourniquet.* *Repeat 1gm for further 2 doses at 8 hourly intervals* **HIGH RISK or SERIOUS PENICILLIN or CEPHALOSPORIN ALLERGY:** - Current or previous MRSA colonisation / infection (within 5 yrs) - Nursing Home resident - Inter-hospital transfer until cleared by IC *VANCOMYCIN plus GENTAMICIN.* *Repeat VANCOMYCIN in 12hours (once only), unless impaired renal function (GFR less than 30ml/min)* **JOINT REVISIONS:** *NO ANTIBIOTICS PRE-OPERATIVELY IF INFECTION SUSPECTED!* *After deep specimens collected administer* *CEPHAZOLIN or if high risk (as above)* *administer VANCOMYCIN plus* *GENTAMICIN* *Post-operatively: continue CEPHAZOLIN or VANCOMYCIN for 5 days while awaiting culture results. Modify therapy based on microscopy and / or culture. If organism known or no specimen required and high risk, use appropriate antibiotic +/-* *VANCOMYCIN*	**REGULAR CYSTOSCOPY +/- BIOPSY OR DIATHERMY:** **NON-INFECTIVE NEPHRECTOMY:** *Antibiotics not required unless another indication present* **HIGH RISK ENDOSCOPIC PROCEDURE:** **NEPHROURETERECTOMY:** **PERCUTANEOUS NEPHROLITHOTOMY:** **RADICAL PROSTATECTOMY:** **RADICAL CYSTECTOMY:** **TURP:** **URETERIC IMAGING OR INSTRUMENTATION:** *GENTAMICIN plus AMPICILLIN* **TRUS BIOPSY:** *CIPROFLOXACIN oral 500mgs 2 hours prior to procedure, repeat 6-12 hours* **ADD GENTAMICIN if high risk** **FEMALE INCONTINENCE SURGERY:** *GENTAMICIN plus AMPICILLIN plus METRONIDAZOLE*	**COLORECTAL SURGERY:** *AMPICILLIN plus GENTAMICIN plus METRONIDAZOLE prior to skin incision.* *If penicillin allergy: use CEFTRIAXONE as solo therapy* **UPPER GASTRO-INTESTINAL SURGERY:** *CEPHAZOLIN* **HERNIA REPAIR WITH MESH:** *CEPHAZOLIN* **HERNIA REPAIR without MESH:** *Antibiotics not required unless another indication present* **ABDOMINOPLASTIES:** **BREAST REDUCTIONS:** **IMPLANT:** **HEAD AND NECK PROCEDURES:** **BONE GRAFTING:** *CEPHAZOLIN before skin incision or before inflation of tourniquet.*

Reminder:
These surgery-specific guidelines pre-suppose antibiotic-specific naïve patient

Standard Dose:

AMPICILLIN DOSAGE	- 1gm
CEPHAZOLIN DOSAGE	- 2gms, one dose only unless otherwise indicated (1gm 8 hourly if continuing)
VANCOMYCIN DOSAGE	- 1gm infused over at least 1 hour prior to procedure (1gm in 250mls; use with infusion pump)
GENTAMICIN DOSAGE	- 3mgs per kg, one dose only, any subsequent doses based on trough level (*consult if already receiving gentamicin*)
METRONIDAZOLE DOSAGE	- 500mgs with infusion completed prior to procedure

ALLERGIES:
Patient allergic to **beta lactams** (penicillins and cephalosporins) AND **vancomycin**, use lincomycin 600mgs infused over 1 hour
Patient allergic to **GENTAMICIN** (rare) used cephazolin or vancomycin or lincomycin.
Serious **PENICILLIN ALLERGY** - immediate type – angio-oedema, urticaria, raised wheals

If further information required (i.e. special or unusual cases): contact FMC Infection Diseases Registrar or Consultant-on-Call on RGH extension 3022 (FMC switchboard)

Authorized:	Unit Head Vascular	Unit Head Orthop.	Unit Head Urology	Unit Head Gen Surg	

Div. Dir.   Date: 15/12/2009

Unit Head Anaes.   Div. Dir.

Government of South Australia
Central Northern Adelaide Health Service

Royal Adelaide Hospital
Approved by the Antibiotic Working Party of the RAH Drug Committee September 2003, August 2008

Empiric treatment of sepsis syndrome for patients at presentation to hospital
Infection plus signs of systemic inflammation, such as: tachycardia, hypotension, fever or hypothermia, tachypnea, leukocytosis, leucopenia

SOURCE	ANTIBIOTIC	TYPE III PENICILLIN HYPERSENSITIVITY (serum sickness-type reactions, rash) For penicillin anaphylaxis, contact Infectious diseases or Clinical Microbiology
SOURCE OF SEPSIS NOT KNOWN	Flucloxacillin 2g IV 4 to 6 hourly PLUS Gentamicin* PLUS Vancomycin^ 1g IV, then refer to vancomycin guidelines	Substitute cephazolin 2g IV 8 hourly for flucloxacillin PLUS Gentamicin* PLUS Vancomycin^ 1g IV
BILIARY OR GASTROINTESTINAL TRACT OR FEMALE GENITAL TRACT	Amoxycillin 2g IV 6 hourly PLUS Gentamicin* PLUS Metronidazole 500mg IV 12 hourly	Use metronidazole 500mg IV BD PLUS ceftriaxone 1g IV once daily For female genital tract, or if infection sexually acquired then add in place of amoxycillin: doxycycline 100mg po BD
URINARY TRACT SOURCE	Amoxycillin 2g IV 6 hourly PLUS Gentamicin*	Use gentamicin alone (no cover for enterococci). If gentamicin contraindicated, use ceftriaxone 1g IV once daily (no cover for pseudomonas or enterococci)
SKIN SOURCE (If ischaemic or diabetic foot ulcers contact ID)	Flucloxacillin 2g IV 6 hourly PLUS Vancomycin^ 1g IV, then refer to vancomycin guidelines	Substitute cephazolin 2g IV 8 hourly for flucloxacillin PLUS Vancomycin^ 1g IV, then refer to vancomycin guidelines
INTRAVASCULAR DEVICES (Including CVC)	Flucloxacillin 2g IV 6 hourly PLUS Gentamicin* PLUS Vancomycin^ 1g IV, then refer to vancomycin guidelines	Substitute cephazolin 2g IV 8 hourly for flucloxacillin PLUS Gentamicin* PLUS Vancomycin^ 1g IV, then refer to vancomycin guidelines
COMMUNITY ACQUIRED PNEUMONIA, FEBRILE NEUTROPENIA	See the respective guidelines on the RAH Intranet	
MENINGITIS	Refer to the Antibiotic Therapeutic Guidelines available from the RAH Intranet: Library section	

*Consult the once daily aminoglycoside chart for dosing and monitoring. If patients have a creatinine clearance ≤20mL/min, contact Infectious Diseases or Clinical Microbiology

^ Infectious diseases approval required after the 3rd dose, please annotate the drug chart as to the indication. *Please refer to the Vancomycin dosing and monitoring guidelines on the intranet.*

Review therapy and modify based on pathogen and susceptibility results or if no improvement after 48 hours

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CONSIDER CONVERSION FROM IV TO ORAL ANTIBIOTICS WHEN ALL THE FOLLOWING APPLY:

- temperature <38°C or improving over 24 hrs
- signs & symptoms improved or resolved
- oral / nasogastric intake tolerated & absorbed
- no diagnostic indication for IV therapy eg. endocarditis, febrile neutropenia, *S. aureus* bacteraemia, meningitis, osteomyelitis
- suitable oral alternative available
- patient likely to be adherent with oral therapy

RPH 70829002

IV TO ORAL SWITCH REGIMENS	
IV	**ORAL**
AMOXYCILLIN 1-2g qid	**AMOXYCILLIN** 500mg-1g tds
AZITHROMYCIN* 500mg daily	**ROXITHROMYCIN** 300mg daily
BENZYLPENICILLIN 1.2-1.8g qid	**AMOXYCILLIN** 1g tds
CEFTRIAXONE* 1g daily	**CEFUROXIME** 500mg bd (chest inf)
CEPHAZOLIN 1-2g tds	**CEPHALEXIN** 500mg-1g tds-qid or **CEFUROXIME** 500mg bd (chest inf)
CIPROFLOXACIN* 200-400mg bd	**CIPROFLOXACIN*** 500-750mg bd
CLINDAMYCIN 450-600mg tds	**CLINDAMYCIN** 450mg tds
FLUCLOXACILLIN 1-2g qid	**FLUCLOXACILLIN** 500mg-1g qid
FLUCONAZOLE* 100-400mg daily	**FLUCONAZOLE*** 100-400mg daily
METRONIDAZOLE 500mg bd	**METRONIDAZOLE** 400mg bd
MOXIFLOXACIN* 400mg daily	**MOXIFLOXACIN*** 400mg daily
TAZOCIN®* 4.5g tds	**AUGMENTIN DUO FORTE®** 875/125mg bd (if Pseudomonas or resistant G-ve d/w MICRO/ID)
TIMENTIN® 3.1g qid	
AMOXYCILLIN 1-2g qid plus **GENTAMICIN** 5mg/kg/day	

*RESTRICTED-REFER TO RPH ELECTRONIC DRUG FORMULARY SYSTEM

**Austin Health
Adult Empiric Antibiotic Guidelines+**

CNS

Bacterial meningitis	• ceftriaxone* 2g IV 12H If the patient is immunosuppressed or Listeria infection is suspected *ADD* benzylpenicillin 1.8 to 2.4g IV 4H
HSV encephalitis	• aciclovir* 10mg/kg IV 8H *(adjust dose if ↓renal function)*

GU tract

UTI and mild pyelonephritis	trimethoprim *OR* cephalexin *OR* Augmentin • Non-pregnant women: 3 to 5 days treatment • Men and pyelonephritis: 14 days treatment • Consider acute or chronic prostatitis: up to 4 weeks treatment
Severe UTI/ pyelonephritis	• ampicillin 2g IV 6H PLUS gentamicin • *If renally impaired:* substitute gentamicin with ceftriaxone* 1g IV daily

GI tract

Upper GI (cholangitis, cholecystitis)	• ampicillin 2g IV 6H *PLUS* gentamicin ± metronidazole 500mg IV 8H • *If renally impaired:* ceftriaxone* 1g IV daily *PLUS* ampicillin ± metronidazole
Peritonitis secondary to perforation	• ampicillin 2g IV 6H *PLUS* gentamicin *PLUS* metronidazole 500 mg IV 8H • *If renally impaired:* Tazocin*
SBP	• ceftriaxone* 1g IV daily *PLUS* ampicillin for 5 days treatment

Skin/soft tissue

Cellulitis	• **Oral:** flucloxacillin 500mg po qid • **IV: HITH candidate:** cephazolin 2g IV daily PLUS probenecid 1g po daily • **In-patient:** flucloxacillin 2g IV 6H

This guideline must not replace clinical judgement. May not apply to paediatrics & immuno-compromised patients.
• Detailed guidelines available in Therapeutic Guidelines: Antibiotic, Version 13 (ABG13)
* Requires ID approval using IDEA³S or contacting ID Reg
+ Doses are for patients with normal renal function

Respiratory

Community-Acquired Pneumonia (with CXR changes)	*Mild CAP: (PSI ≤70 = Class I/II)* • amoxycillin 0.5g to 1g po 8H *PLUS* doxycycline 100mg po 12H for 5 days treatment
• Calculate Pneumonia Severity Index (PSI) using IDEA³S computer program	*Moderate CAP: (PSI 71 - 90 = Class III, 91 - 130 = Class IV)* • benzylpenicillin 1.2g IV 6H *PLUS* doxycycline 100mg po 12H for 5 to 7 days treatment
• Hospital-acquired Pneumonia see ABG13	*Severe CAP: (PSI > 130 = Class V, or patients requiring ICU management):* • ceftriaxone* 1g IV daily *PLUS* azithromycin 500mg IV daily
Infective exacerbation of COPD *Cardinal symptoms:* ↑ dyspnoea ↑ sputum volume ↑ sputum purulence	*2 to 3 symptoms:* • doxycycline100mg po 12H or amoxycillin 500mg po 8H *If unable to swallow or altered conscious state or new infiltrate on CXR:* • benzylpenicillin 1.2g IV 6H *PLUS* doxycycline 100 mg po 12H *1 symptom:* • Antibiotics are of no benefit

Timely conversion from IV to oral agents

Re-assess the need for IV antibiotic administration in your patient if the following exist:

- Temperature <38°C for 2 days
- Oral food and fluids tolerated
- No ongoing or potential absorption problems
- No unexplained tachycardia
- Oral formulation or suitable oral alternative available. Check with ward pharmacist.
- Oral therapy is often not suitable for patients with endocarditis, meningitis, osteomyelitis/ septic arthritis, Staph. aureus bacteraemia where a high tissue antibiotic concentration is required.

Expires May 2010

A Quick Guide to SWITCH!

Antibiotics: IV to Oral

Benefits of Early Switch to Oral Therapy

- Decreased risk of complications from IV lines: thrombophlebitis, catheter related infections
- More patient friendly (improves mobility and comfort)
- May lead to earlier discharge
- Saves medical and nursing time
- Reduction in costs: Direct - medication
                            Indirect – diluents, equipment, needles

A Melbourne hospital that implemented a similar campaign estimated they saved nearly $100,000 per annum in medication costs alone, simply by reducing excess IV antibiotic use.

Safety of Switching

A large number of clinical trials support early switching to oral antibiotics, following **two to three** days of treatment with IV therapy[1],[2]

- Equal treatment efficacy
- No adverse effects on patient outcome

Criteria for Switching

- Oral fluids/foods are tolerated and no reason to believe that poor oral absorption may be a problem e.g. vomiting, diarrhoea
- Temperature less than 38°C for 24 to 48 hours
- No signs of sepsis
- An appropriate oral antibiotic is available
- Extra high tissue antibiotic concentrations or a prolonged course of IV antibiotics are not essential

Conditions where SWITCH should be considered

- Gram negative bacteraemia
- Hospital acquired infections
- Intra-abdominal infections
- Pneumonia
- Skin and soft tissue infections
- Urinary tract infections

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[1] Barlow GD, Nathwani D. Sequential Antibiotic Therapy. Curr Opin Infect Dis. 2000; 13(6):599-607
[2] Sevinc F et al. Early Switch from Intravenous to Oral Antibiotics: Guidelines and Implementation in a Large Teaching Hospital. J Antimicrob Chemother. 1999; 43:601-606

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Conditions where SWITCH is not appropriate

Conditions which require a prolonged course of IV antibiotics or very high tissue concentrations

- Bone and joint infections
- Cystic fibrosis
- Endocarditis
- Deep seated abscess
- Meningitis
- *S. aureus* bacteraemia

Antimicrobials with Excellent Oral Bioavailability

Fluconazole (>90%)
Ciprofloxacin (70-80%)
Metronidazole (>95%)

Moxifloxacin (~90%)
Clindamycin (~90%)

Suggested Conversion Regimens

Refer to *Therapeutic Guidelines: Antibiotic* for dosing in specific indications

IV		Oral	
Antimicrobial	**Usual Dose***	**Antimicrobial**	**Usual Dose***
Ampicillin	1-2g IV QID	Amoxycillin	500mg-1g oral TDS
Azithromycin	500mg IV Daily	Roxithromycin	300mg oral daily
Benzyl penicillin	1.2g IV QID	Phenoxymethyl penicillin	500mg oral QID
Ceftriaxone	1g IV Daily	No oral formulation Choice of oral antibiotic depends on infection site/microbiology	
Cephazolin	1g IV TDS	Cephalexin	500mg oral QID
Ciprofloxacin^	200-400mg IV BD	Ciprofloxacin^	250-500mg oral BD
Flucloxacillin	1g IV QID	Flucloxacillin	500mg oral QID
Lincomycin	600-900mg IV TDS	Clindamycin^	300-600mg oral TDS
Fluconazole^	200-400mg IV daily	Fluconazole^	200-400mg oral daily
Metronidazole^	500mg IV BD	Metronidazole^	400mg oral TDS

*Usual dose for adult patients with normal renal function.
^Antimicrobials with excellent oral bioavailability

For further information contact:

Your ward pharmacist
Infectious diseases registrar/consultant
Infectious diseases pharmacist   Pager 4325
                                        Ext 41364

Southern Health

Southern Health Therapeutics Committee
Southern Health Pharmacy Department
AMPS Committee

SWITCH!
ANTIBIOTICS - IV to ORAL
GUIDELINES FOR WARD PHARMACISTS

WHAT IS THE SWITCH CAMPAIGN?
The Switch Campaign is being implemented at Southern Health in 2009. It encourages a timelier switch from IV to oral antibiotics, in appropriate patients.

WHY SWITCH?
- Decreased risk of infection from IV lines
- Decreased risk of thrombophlebitis
- Significantly less expensive than IV therapy
- Reduction in hidden costs (diluents, equipment, needles, nursing time)
- More patient friendly
- May lead to earlier discharge

WHAT ARE THE CRITERIA FOR SWITCHING FROM IV TO ORAL?
- Oral fluids/foods are tolerated and no reason to believe that poor oral absorption may be a problem e.g. vomiting, diarrhoea
- Temperature less than 38°C for 24 to 48 hours
- No signs of sepsis
- An appropriate oral antibiotic is available
- Extra high tissue antibiotic concentrations or a prolonged course of IV antibiotics are <u>not</u> essential*
  *N.B.: Some conditions require a prolonged course of IV antibiotics or very high tissue concentrations e.g. bone and joint infections, endocarditis, meningitis, *S. aureus* bacteraemia, cystic fibrosis, deep seated abscess

WHEN SHOULD SWITCH BE CONSIDERED?
- Gram negative bacteraemia
- Hospital acquired infections
- Intra-abdominal infections
- Pneumonia
- Skin and soft tissue infections
- Urinary tract infections

Antimicrobial choice should always be guided by microbiology sensitivities when available.

PHARMACIST CAMPAIGN KIT
- Guidelines for ward pharmacists (to be kept in ward pharmacist's folder)
- Lanyard tags (for doctors and pharmacists)
- Posters (to be displayed on ward and a copy for ward pharmacist's folder)
- Intervention stickers (for use on medication chart and pharmacy communication form)
- Leaflets for prescribers – "A Quick Guide to Switch"

Southern Health

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WARD PHARMACIST ROLE

The successful implementation of this campaign will rely predominately on the ward pharmacist.

What to do:

Place switch campaign posters on ward notice boards.

Educate medical and nursing staff (leaflets, lanyard tags and verbal communication).

Proactively discuss switching options with medical staff.

Steps:

1. Assess all IV antibiotic orders for appropriateness of switching to oral therapy (during daily medication chart review) – **refer to flow chart.**

If appropriate to switch:

2. Place switch sticker on medication chart (place in section ensuring that you do not obscure or obstruct nursing administration signatures).
3. Use communication sticker on pharmacy communication form and suggest appropriate oral antimicrobial therapy.
4. Communicate this information with the medical officer (e.g. lanpage, verbally).
5. Ensure that Southern Health Traffic Light Antimicrobial Prescribing Restrictions are met. (e.g. ID approval numbers).

USEFUL CONTACTS

ID registrar

ID pharmacist: extension 41364 or pager 4325

EXAMPLES OF DOCUMENTATION

Flowchart for Identification of Patients Suitable
for Early Switch to Oral Antibiotics

```
                    ┌─────────────────────────────┐
                    │ Patient prescribed IV        │
                    │ antibiotic(s)                │
                    │ Is the indication suitable   │
                    │ for an early switch to oral  │
                    │ antibiotics?*                │
                    └─────────────────────────────┘
                      │                      │
              ┌───────────┐          ┌───────────┐
              │    No     │          │    Yes    │
              └───────────┘          └───────────┘
                    │                      │
      ┌──────────────────────┐    ┌─────────────────────┐
      │ Continue current     │    │ Is the patient       │
      │ management with ID   │    │ tolerating oral      │
      │ involvement as       │    │ food/fluids?         │
      │ necessary            │    │ No vomiting/diarrhoea│
      └──────────────────────┘    └─────────────────────┘
                                     │              │
                             ┌───────────┐   ┌───────────┐
                             │    No     │   │    Yes    │
                             └───────────┘   └───────────┘
```

Is patient afebrile?
Temperature <38°C for 24 - 48hrs

No   Yes

Are sepsis markers showing **trend** toward normal?
Not more than one of the following:
WCC <4 or >12 x10^{9}/L
BP unstable or hypotension
RR >20 breaths/min
Heart rate >90 bpm

No   Yes

Is an appropriate oral antibiotic available?

No   Yes

Continue IV antibiotics with daily review.
ID referral may be appropriate

Patient is suitable to switch to oral antibiotics

* Some conditions require <u>prolonged course of IV antibiotics OR high tissue concentration</u>, so are not suitable for early switch.
  E.G. Bone/joint infections, endocarditis, meningitis, *S. aureus* bacteraemia, cystic fibrosis, deep seated abscess

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ANTIMICROBIAL COSTS AND SAVINGS

Refer to *Therapeutic Guidelines: Antibiotic* for dosing in specific indications

If no equivalent oral formulation available choice of antimicrobial should be based on site of infection, microbiology or ID consultation.

IV		Oral		Saving per 24 hours
Antimicrobial/ usual dose*	Cost per 24 hours	Antimicrobial/ usual dose*	Cost per 24 hours	
Ampicillin 1-2g IV QID	$4.32	Amoxycillin 500mg-1g oral TDS	$0.24	$4.08
Azithromycin 500mg IV daily	$25.00	Azithromycin 500mg oral daily	$7.07	$17.93
		Roxithromycin 300mg oral daily	$0.42	$24.58
Benzyl penicillin 1.2g IV QID	$19.12	Phenoxymethyl penicillin 500mg oral QID	$0.52	$18.60
Ceftriaxone 1g IV daily	$2.00	Amoxycillin/ Clavulanic acid# 875/125mg oral BD	$0.84	$1.16
Cephazolin 1g IV TDS	$5.79	Cephalexin 500mg orally QID	$0.72	$5.07
Ciprofloxacin^ 200-400mg IV BD	$30.00	Ciprofloxacin^ 250-500mg oral BD	$0.72	$29.28
Flucloxacillin 1g IV QID	$4.76	Flucloxacillin 500mg oral QID	$0.76	$4.00
Fluconazole^ 200-400mg IV daily	$19.90	Fluconazole^ 200-400mg oral daily	$2.60	$17.30
Lincomycin^ 600-900mg IV TDS	$24.96	Clindamycin^ 300-600mg oral TDS	$4.23	$20.73
Metronidazole^ 500mg IV BD	$5.80	Metronidazole^ 400mg oral TDS	$0.33	$5.47
Moxifloxacin 400mg IV daily	$70.05	Moxifloxacin 400mg oral daily	$11.37	$58.68
Piperacillin/ tazobactam 4.5g IV TDS	$47.85	Amoxycillin/ clavulanic acid 875/125mg oral BD	$0.84	$47.01
Ticarcillin/ clavulanic acid 3.1g IV QID	$42.96	Amoxycillin/ clavulanic acid 875/125mg oral BD	$0.84	$42.12

*Usual dose for adult patients with normal renal function

Ensure patient does not have penicillin hypersensitivity

^Antimicrobials with excellent oral bioavailability

Reviewed by: Infectious Diseases Pharmacists	Last Review Date: October 2009
Authorised by: AMPS Committee	Next Review Date: October 2012

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Appendixes — Resource materials

Getting to know your Penicillins

⚠️ ⚠️

Does Tazocin contain Penicillin?
What's in Augmentin?

We need to be familiar with which drugs contain penicillin so that we don't expose our Penicillin allergic patients to any unnecessary risk.

AUGMENTIN   TAZOCIN   TIMENTIN

**These drugs cause problems because their names do not immediately
suggest that they contain penicillin.**

See table for commonly used Penicillins

Generic Name	Brand Name
Amoxycillin	Amoxil, Alphamox, Cilamox, Moxacin
Ampicillin	Alphacin, Ampicyn
Benzylpenicillin	Ben Pen
Dicloxacillin	Diclocil
Flucloxacillin	Flopen, Floxapen, Staphylex
Phenoxymethylpenicillin	Abbocillin VK, Cilicaine VK.
Piperacillin	Piperacillin
Procaine Penicillin	Cilicaine

Commonly used combination products;

Amoxycillin + Clavulanic Acid	Augmentin, Curam, Clamoxyl
Piperacillin + Tazobactam	Tazocin
Ticarcillin + Clavulanic Acid	Timentin

Specialist Advisory Committee on Antimicrobial Resistance (SACAR) template for hospital antimicrobial guidelines (Specialist Advisory Committee on Antimicrobial Resistance (SACAR) 2007)

Antimicrobial guidelines should be evidence-based and prepared in line with best practice recommendations for treatment guidelines. The provision of costing information within the guideline should be discussed locally. The following are additional recommendations for the content and details of local antimicrobial policies.

8.1   Title page

- Name of policy
- Specify the condition and patient group where appropriate
- Date
- Version
- Review date
- Authors
- Contact details for enquiries for normal hours and out of hours
- Contact details for microbiological and pharmacological information
- Details of electronic availability

8.2   Introduction section

- Statement as to whether the guideline is mandatory or for guidance only
- Contents
- Guidance on the loal procedure for microbiological samples
- Abbreviations used in the text
- Reference should be made to guidance in the British National Formulary under Prescription writing. These notes lay out a standard for expressing strengths and encourage directions in English not Latin abbreviations

8.3   Summary list of available antimicrobials

The antimicrobials that are recommended in the guidelines should be listed, with clear indications to the route of administration and should state whether they are:

- Unrestricted
- Restricted (approval of a specialist is required)
- Permitted for specific conditions (for example co-trimoxazole for *Pneumocystis*)

8.4 *Regimens for treatment of common infections*

8.4.1 *Treatment*

- First-line recommendation
- Second-line recommendation
- Timing
- Dose
- Route of administration
- Duration of treatment
- Rules for intravenous to oral switch

8.4.2 *Prophylaxis*

- First-line recommendation for empirical therapy
- Second-line recommendation for empirical therapy
- Dose
- Timing of initial dose
- Route of administration
- Details of repeat dosing if required

Specialist Advisory Committee on Antimicrobial Resistance (SACAR) (2007). "Appendix 2.Specialist Advisory Committee on Antimicrobial Resistance (SACAR) Antimicrobial Framework " Journal of Antimicrobial Chemotherapy **60**(Suppl.1): i87-i90.

A2.2 Guidance on managing conflicts of interest and relationships with the pharmaceutical industry

The relationship between the pharmaceutical industry and South Australian public hospitals. South Australian Therapeutics Advisory Group, September 2008
www.dassa.sa.gov.au/webdata/resources/files/SATAG_Guidance_Doc__ Relationship_with_Pharma_2008_9.pdf

Pharmaceutical company representatives — Queensland Health standards of interaction and behaviour. Queensland Health, September 2006
www.health.qld.gov.au/qhcss/mapsu/documents/health_prof/31722.pdf

Pharmaceutical industry and hospital staff liaison in public hospitals. NSW Therapeutic Advisory Group Inc, July 2008
www.ciap.health.nsw.gov.au/nswtag/publications/posstats/Pharmliaison0708.pdf

Liaison between public hospital staff and the pharmaceutical industry: guidance from the NSW Therapeutic Advisory Group. Medical Journal of Australia, April 2009
www.mja.com.au/public/issues/190_08_200409/shi11384_fm.pdf

Conflicts of interest and gifts and benefits. NSW Health 2010
www.health.nsw.gov.au/policies/pd/2010/pdf/PD2010_010.pdf

New physician guidelines on commercial relationships. *WHO Drug Information* 2004;18(4):296–297

Good medical practice: a code of conduct for doctors in Australia. Australian Medical Council, 2009
goodmedicalpractice.org.au

Guidelines for ethical relationships between physicians and industry. The Royal Australasian College of Physicians, 2006
www.racp.edu.au/index.cfm?objectid=CFE4807D-A18C-8144-DCAA3E43107218FB

Doctors' relationships with industry – 2010. Australian Medical Association
ama.com.au/node/5421

Code of professional conduct. Pharmaceutical Society of Australia, 1998
www.psa.org.au/site.php?id=628

Code of conduct. Medicines Australia (Edition 15, 2006; Edition 16, 2010)
www.medicinesaustralia.com.au/pages/page5.asp

A guide to relationships between health consumer organisations and pharmaceutical companies.
www.medicinesaustralia.com.au/pages/images/MA-WorkingTogether-TheGuide.pdf

A2.3 Antimicrobial stewardship web sites

Organisation/ site name	URL	Content and function
National organisations		
Healthcare Infection Control Special Interest Group	www.asid.net.au/hicsigwiki/index. php?title+Antibiotic-Stewardship- programs#guides	An Australian and New Zealand site. Provides a good example of multidisciplinary antimicrobial stewardship, including information such as guidelines, presentations, teaching materials and a large number of related links
Scottish Antimicrobial Prescribing Group	www.scottishmedicines.org.uk/ smc/6616.html	Minutes of meetings, information about educational events, policies, guidance and other key documents relating to antimicrobial management in Scotland
Centers for Disease Control and Prevention	www.cdc.gov/drugresistance/ healthcare/default.htm	Teaching materials and tools to download, including tools for clinicians, from the Centers' Campaign to Prevent Antimicrobial Resistance
Prudent Antibiotic User Website	www.pause-online.org.uk/	Standardised web-based learning resources and assessments on prudent antimicrobial prescribing. A collaborative web-based forum for sharing experiences and learning resources between providers of education
Australian Commission on Safety and Quality in Health Care	www.safetyandquality.gov.au/ internet/safety/publishing.nsf/ Content/PriorityProgram- 03#five	Antimicrobial stewardship committee activities, seminar reports, presentations, program requirements and strategies
The Joint Commission	www.jcrinc.com/Antibiotic- Stewardship/	Online learning community on multiresistant organisms and antibiotic resistance. Includes antimicrobial stewardship educational material
Institutions		
The Nebraska Medical Center	www.nebraskamed.com/careers/ education/asp/	Institutional antimicrobial stewardship program including information on antimicrobial restrictions, guidelines, clinical pathways and pharmacokinetics
Hospital of the University of Pennsylvania	www.uphs.upenn.edu/bugdrug	Institutional antimicrobial stewardship program including information on guidelines for antimicrobial therapy, issues relating to formulary restrictions and pharmacologic considerations for dose adjustments
University of Kentucky Chandler Medical Center	www.hosp.uky.edu/pharmacy/ amt/default.html	Institutional antimicrobial stewardship program including information on policies and guidelines, clinical pathways, ordering procedures for restricted antimicrobials, antibiograms, and a text pager messaging tool for the antimicrobial team

Glossary

antibiogram	The result of laboratory testing for the sensitivity of an isolated bacterial strain to different antibiotics. Antibiograms can be collated to form cumulative antibiograms, which can help to form prescribing guidelines at a hospital, regional or national level.
antibiotic	A substance that kills or inhibits the growth of bacteria.
antimicrobial	A substance that kills or inhibits the growth of microorganisms such as bacteria, viruses or fungi. (See also: antibiotic, which is a class of antimicrobials.)
bacteraemia	A bacterial infection of the blood or the lymph system.
bloodstream infection	The presence of live pathogens in the blood, causing an infection. (See also: pathogen, infection.)
care bundle	A set of evidence-based practices that have been shown to improve outcomes when performed collectively and consistently. The concept was developed by the Institute for Healthcare Improvement in the United States to improve the care process and patient outcomes.
catheter	A thin, flexible, hollow tube used to add or remove fluids from the body.
colonisation	A process in which an organism (such as a bacterium) grows inside someone without causing illness.
control	A standard against which other conditions can be compared in a scientific experiment. For example, if an experiment tested the effects of a new antimicrobial, the results might be compared against a control group of people given standard antimicrobials.
epidemiology	The study of factors that have an impact on disease in the human community. Often used in the control of health problems.
healthcare associated infection (HAI)	Infections acquired as a direct or indirect result of health care.
immunocompromised	Having an immune system that has been impaired by disease or treatment.
infection	The invasion and reproduction of pathogenic (disease-causing) organisms inside the body. This can cause tissue injury and progress to disease.
infection control or infection control measures	Measures that aim to prevent the spread of pathogens between people in a healthcare setting. Examples of infection control measures include hand washing, protective clothing, isolation procedures and audits of compliance with hygiene measures.
inpatient	A patient who visits a healthcare facility for diagnosis or treatment and stays in the hospital for at least one night.
intravenous	Within or into a vein (e.g. an intravenous catheter would be a catheter that is inserted into a vein).

morbidity	The state of being ill, diseased or injured. ('Morbidity rate' describes the occurrence of a disease or condition that causes morbidity.)
mortality	Death, or the frequency or number of deaths. For example: infections are a major cause of mortality worldwide, and the mortality rate of [this type of] infection is 30%.
nosocomial infection	An infection acquired in hospital.
occupied bed-days (OBDs)	Total number of bed-days of all admitted patients accommodated during the reporting period, taken from a count of the number of inpatients at about midnight each day. Details for patients being admitted and leaving on the same day are also recorded as OBDs, counting one OBD for each same-day patient. In the United States, OBDs are referred to as 'patient days'.
outbreak	A classification used in epidemiology to describe a small, localised group of people infected with a disease.
outpatient	A patient who visits a healthcare facility for diagnosis or treatment without spending the night. Sometimes called a day patient, day-stay patient or day-only patient.
pathogen	A disease-causing agent. The term is often used to refer to infectious microorganisms, such as bacteria, viruses or fungi.
prophylactic	Medications or treatments that are preventive in the treatment of disease. For example, antimicrobials are sometimes given prophylactically before surgery to prevent infection.
risk factor	An activity or factor that may increase the chance of developing a disease. For example, smoking is a risk factor for lung cancer.
sepsis	A serious medical condition that is characterised by a whole-body inflammatory state (called a systemic inflammatory response syndrome or SIRS) and the presence of a known or suspected infection.
strain	A strain is a genetic variant or subtype of a microorganism (e.g. a virus, bacterium or fungus). Some strains may be more dangerous or difficult to treat than others.
surgical site infection	An infection at the site of a surgical operation that is caused by the operation.
surveillance	Disease surveillance is an epidemiological practice by which the spread of disease is monitored in order to establish patterns of progression. The main role of disease surveillance is to predict, observe and minimise the harm caused by outbreak, epidemic and pandemic situations, as well as increase our knowledge as to what factors might contribute to such circumstances.

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